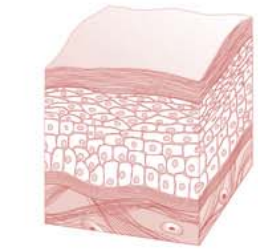
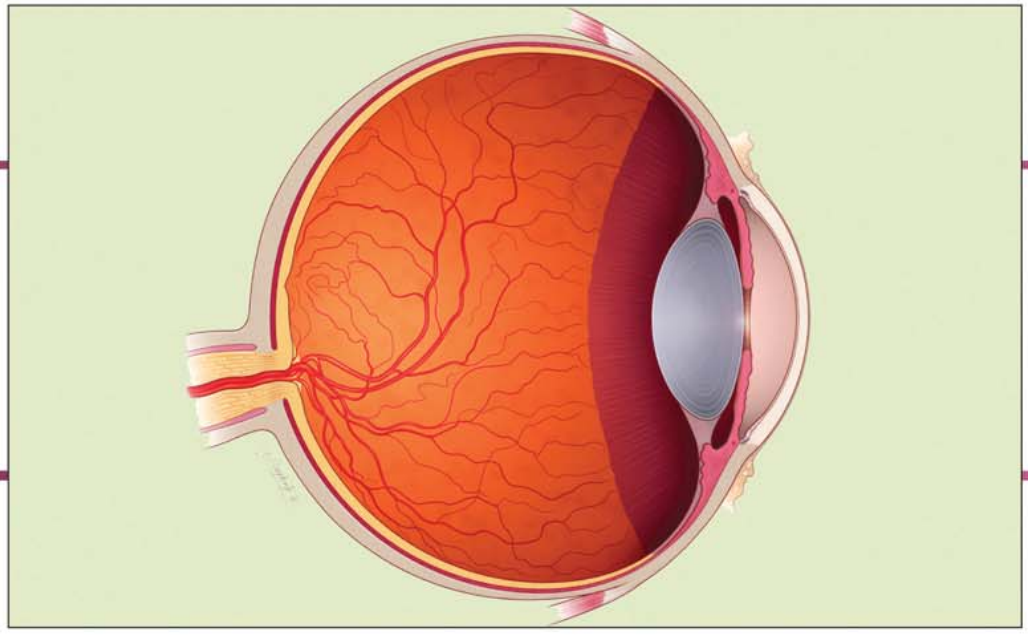
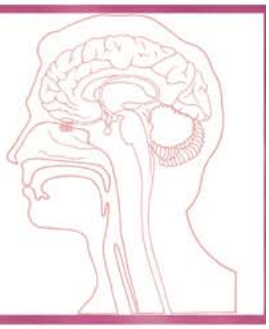
THE FACTS ON FILE ENCYCLOPEDIA OF

Health and Medicine







A Comprehensive and Concise Guide to the Human Body and Modern Medical Practices

VOLUME 1

THE FACTS ON FILE ENCYCLOPEDIA OF

HEALTH AND MEDICINE

IN FOUR VOLUMES:

VOLUME 1

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HEALTH AND MEDICINE

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VOLUME 1

An Amaranth Book

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To your health!

The information presented in *The Facts On File Encyclopedia of Health and Medicine* is provided for research purposes only and is not intended to replace consultation with or diagnosis and treatment by medical doctors or other qualified experts. Readers who may be experiencing a condition or disease described herein should seek medical attention and not rely on the information found here as medical advice.

The Facts On File Encyclopedia of Health and Medicine in Four Volumes: Volume 1

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VOLUME 1

FOREWORD

A big part of my role as a physician is educating my patients about their health. I take as much time as each person needs to explain prevention measures, test results, and treatment options. I encourage questions. But in the moment, sitting there in my office, most people do not yet know what to ask me. By the time questions flood their thoughts, they may be back at work or at home.

Numerous events and circumstances can challenge health, and we all need to know what actions we can take to keep ourselves healthy as well as to obtain appropriate treatment for health conditions that do affect us. Knowledge empowers all of us to make informed and appropriate decisions about health care. Certainly there is no shortage of reference material. Yet there is *so* much information available today! Even for physicians, it is challenging to keep up. How can you get to the core of what you want to know, reliably and to the level of detail you need?

The Facts On File Encyclopedia of Health and Medicine is a great resource for up-to-date health information presented in a manner that is both comprehensive and easy to understand no matter what your level of medical knowledge. The encyclopedia organizes entries by body system. The progression of body systems—and entries—throughout the encyclopedia presents topics the way you think about them.

Going beyond this basic structure, however, is another layer of organization that particularly appeals to me, which is a comprehensive structure of cross references that integrates entries across body systems. After all, your body functions in an integrated way; so, too, should a reference series that discusses your body's health. Not very much that happens with your health affects one part of your body in isolation from other body structures and functions. Your body attempts to compensate and adjust, often without your awareness, until it can no longer accommodate the injury or illness. The symptoms you bring to your doctor may reflect this compensation, for example frequent headaches that point not to brain tumor (as many people fear but is very rare) but to eye strain or muscle tension or sometimes to hypertension (high blood pressure).

In my medical practice I emphasize integrative health care, embracing the philosophy that health exists as the intricate intertwining of the body's many systems, structures, and functions. So, too, does the care of health. I received my medical degree from Tufts University School of Medicine in Boston, an institution noted for remaining at the forefront of the medical profession. I also completed clinical programs in Mind-Body Medicine at Harvard University, Integrative Medicine at the University of Arizona School of Medicine, and Medical Acupuncture at the University of California-Los Angeles (UCLA). I am a board-certified obstetrician-gynecologist, a board-certified clinical nutritionist, and a licensed acupuncturist. I see patients in my practice in Cincinnati, Ohio; I teach, I lecture, and I frequently go on television and radio to talk about health topics. In each of these areas, I encourage people to think about their health and health concerns from an integrative perspective. When you understand your health from multiple dimensions, you can better understand what to do to keep yourself as healthy as possible.

I wish you the best of health for all of a long, satisfying life. But when the time comes that you must make decisions about medical care, I want you to have the knowledge to make informed

choices that are right for you. Whether you start here and move on to more specialized resources or locate all the information you need within these four volumes, you will find *The Facts On File Encyclopedia of Health and Medicine* to be a most valuable reference resource.

—Maureen M. Pelletier, M.D., C.C.N., F.A.C.O.G.

HOW TO USE
THE FACTS ON FILE ENCYCLOPEDIA OF HEALTH AND MEDICINE

Welcome to *The Facts On File Encyclopedia of Health and Medicine*, a four-volume reference set. This comprehensive resource is an indispensable reference for students, allied health professionals, physicians, caregivers, lay researchers, and people seeking information about health circumstances and conditions for themselves or others. Entries present the latest health concepts and medical knowledge in a clear, concise format. Readers may easily accumulate information and build a complete medical profile on just about any health or medical topic of interest or concern.

A New Paradigm for the Health and Medical Encyclopedia

As the art and science of health and medicine continues to evolve, with complex and elegant discoveries and new techniques, medications, and treatments emerging all the time, the need has arisen for a new paradigm for the encyclopedia of health and medicine—a rethinking of the old, and increasingly outmoded, presentations. Carefully researched and compiled, *The Facts On File Encyclopedia of Health and Medicine* offers many distinguishing features that present readers and researchers with an organization as up-to-date and compelling as the breakthrough information its entries contain.

Recognizing the current emphasis on presenting a truly integrative approach to both health and disease, *The Facts On File Encyclopedia of Health and Medicine* organizes content across volumes within a distinctive format that groups related entries by body system (for example, "The Cardiovascular System") or by general health topic (for example, "Genetics and Molecular Medicine"):

- **Volume 1** presents the sensory and structural body systems that allow the body to engage with its surroundings and the external environment.
- **Volume 2** presents the cell- and fluid-based body systems that transport nutrients, remove molecular wastes, and provide protection from infection.
- **Volume 3** presents the biochemical body systems that support cellular functions.
- **Volume 4** presents topics that apply across body systems (such as "Fitness: Exercise and Health") or that address broad areas within health care (such as "Preventive Medicine").
- The appendixes provide supportive or additional reference information (such as "Appendix X: Immunization and Routine Examination Schedules").

Following Research Pathways

The Facts On File Encyclopedia of Health and Medicine's organization and structure support the reader's and researcher's ease of use. Many encyclopedia users will find all the information they desire within one volume. Others may use several or all four of the encyclopedia's volumes to arrive at a comprehensive, multifaceted, in-depth understanding of related health and medical concepts and information. Researchers efficiently look up information in *The Facts On File Encyclopedia of Health and Medicine* in several ways.

Each section's entries appear in alphabetical order (except the entries in Volume 4's "Emergency and First Aid" section, which are grouped by type of emergency). The researcher finds a desired entry by looking in the relevant volume and section. For example, the entry for **acne** is in Volume 1 in the section "The Integumentary System" and the entry for **stomach** is in Volume 3 in

the section "The Gastrointestinal System." The researcher can also consult the index at the back of the volume to locate the entry, then turn to the appropriate page in the volume.

Terms that appear in SMALL CAPS within the text of an entry are themselves entries elsewhere in *The Facts On File Encyclopedia of Health and Medicine*. Encyclopedia users can look up the entries for those terms as well, for further information of potential interest. Such SMALL CAPS cross references typically provide related content that expands upon the primary topic, sometimes leading the user in new research directions he or she might otherwise not have explored.

For example, the entry **hypertension** is in the section "The Cardiovascular System." The entry presents a comprehensive discussion of the health condition hypertension (high blood pressure), covering symptoms, diagnosis, treatment options, risk factors, and prevention efforts. Among the numerous SMALL CAPS cross references within the hypertension entry are the entries for

- **retinopathy**, an entry in the section "The Eyes" in Volume 1, which discusses damage to the eye that may result from untreated or poorly managed hypertension
- **blood pressure**, an entry in the Volume 2 section "The Cardiovascular System," which discusses the body's mechanisms for maintaining appropriate pressure within the circulatory system
- **stroke** and **heart attack**, entries in Volume 2's "The Cardiovascular System" about significant health conditions that may result from hypertension
- **kidney,** an entry in the section "The Urinary System" in Volume 3, which discusses the kidney's role in regulating the body's electrolyte balances and fluid volume to control blood pressure
- **atherosclerosis, diabetes, hyperlipidemia,** and **obesity**, entries in the sections "The Cardiovascular System" in Volume 2, "The Endocrine System" in Volume 3, and "Lifestyle Variables: Smoking and Obesity" in Volume 4, and all of which are health conditions that contribute to hypertension

Following the path of an encyclopedic entry's internal cross references, as shown above, can illuminate connections between body systems; define and apply medical terminology; reveal a broad matrix of related health conditions, issues, and concerns; and more. The SMALL CAPS cross references indicated within the text of encyclopedic entries lead encyclopedia users on wide-ranging research pathways that branch and blossom.

At the end of the entry for **hypertension** a list of cross references gathered in alphabetical order links together groups of related entries in other sections and volumes, such as **smoking cessation** in Volume 4's "Lifestyle Variables: Smoking and Obesity," to provide specific, highly relevant research strings. These *see also* cross references also appear in SMALL CAPS, identifying them at a glance. Encyclopedia users are encouraged to look here for leads on honing research with precision to a direct pathway of connected entries.

So, extensive cross-references in *The Facts On File Encyclopedia of Health and Medicine* link related topics within and across sections and volumes, in both broad and narrow research pathways. This approach encourages researchers to investigate beyond the conventional level and focus of information, providing logical direction to relevant subjects. Each cross-referenced entry correspondingly has its own set of cross references, ever widening the web of knowledge.

Using the Facts On File Encyclopedia of Health and Medicine

Each section of the encyclopedia begins with an overview that introduces the section and its key concepts, connecting information to present a comprehensive view of the relevant system of the human body or health and medical subject area. For most body systems, this overview begins with a list and drawings of the system's structures and incorporates discussion of historic, current, and future contexts.

Entries present a spectrum of information from lifestyle factors and complementary methods to the most current technologic advances and approaches, as appropriate. Text that is set apart or bold within an entry gives an important health warning, or targets salient points of interest to add layers of meaning and context. Lists and tables

collect concise presentations of related information for easy reference.

Each type of entry (mid-length and longer) incorporates consistent elements, identified by standardized subheadings:

- ***Entries for health conditions and diseases*** begin with a general discussion of the condition and its known or possible causes and then incorporate content under the subheadings "Symptoms and Diagnostic Path," "Treatment Options and Outlook," and "Risk Factors and Preventive Measures."
- ***Entries for surgery operations*** begin with a general discussion of the procedure and then incorporate content under the subheadings "Surgical Procedure," "Risks and Complications," and "Outlook and Lifestyle Modifications."
- ***Entries for medication classifications*** begin with a general discussion of the type of medication and its common uses and then incorporate content under the subheadings "How These Medications Work," "Therapeutic Applications," and "Risks and Side Effects."
- ***Entries for diagnostic procedures*** begin with a general discussion of the test or procedure and then incorporate content under the subheadings "Reasons for Doing This Test," "Preparation, Procedure, and Recovery," and "Risks and Complications."

Entries in Volume 4's section "Emergency and First Aid" are unique within the orientation of *The Facts On File Encyclopedia of Health and Medicine* in that they feature instructional rather than informational content. **These entries do *not* replace appropriate training in emergency response and first aid methods.** Rather, these entries provide brief directives that are appropriate for guiding the actions of a person with little or no first aid training who is first on the scene of an emergency.

Each volume concludes with a complete, full index for the sections and entries within the volume. Volume 4 of *The Facts On File Encyclopedia of Medicine* contains a comprehensive index for all four encyclopedia volumes that researchers can use to quickly and easily determine which volumes contain desired sections or entries.

The Facts On File Encyclopedia of Health and Medicine in Four Volumes

PREFACE TO VOLUME 1

Leading the reader into the four-volume *The Facts On File Encyclopedia of Health and Medicine* through Volume 1 are the structures and functions that lead the body's way in the world. These are the body systems that equip the body to interact with its external environment. Some people refer to these as the "interface" systems, drawing from the concepts and terminology of computers. These systems allow the body to receive and respond to sensory input.

The Ear, Nose, Mouth, and Throat

Volume 1's first section is the "The Ear, Nose, Mouth, and Throat." Through these structures the body receives auditory, olfactory, and gustatory sensory information—sounds, smells, and tastes. The throat does double duty as the conduit to carry both air and nutrition, essential sustenance for the body, and also makes possible the uniquely human form of communication—speech.

The functions of these sensory organs and structures overlap and integrate with each other in ways such that the loss of one sensory system affects others. Speech is difficult without the ability to hear, for example, and the sensory pathways for smell and taste are so intertwined that both networks become impaired when one or the other does not function properly. Olfactory nerve fibers are capable of detecting thousands of odors, enhancing the brain's ability to interpret hundreds of flavors with input from only four basic taste qualities (sweet, sour, salt, and bitter).

The sense of touch resides in specialized nerves that populate the surface of the skin in varying concentrations to provide different levels of tactile response. The lips and fingertips, for example, are exquisitely sensitive, while the surfaces of the arms and legs are less responsive to touch. The structures of the inner ear also regulate the body's balance, integrating with the nervous system as well as the musculoskeletal system (as anyone who has found it challenging to walk after spinning in circles well knows).

The Eyes

Sight is so highly refined in humans that many people consider it the most important of the five senses. The structures of vision function independently from other sensory structures, though the brain combines sensory information to develop complex perspectives about the body's placement and function within its external environment.

The two eyes work independently as well, though synchronously. The brain blends and interprets the information it receives from each eye to form images that have spatial dimension. This provides depth perception, which interplays with proprioception (the body's sense of its placement within its physical environment) and movement. The loss of vision in one eye requires the brain to rely more on other sensory input and on learned responses to help the body navigate in a dimensional world.

The Integumentary System

The structures of the integumentary system—skin, nails, and hair—cover and protect the body from the external environment as well as provide the basis for appearance and identity. Integument is Latin for "cloak," an apt term for the system that envelops the body and literally holds it together.

The integumentary system provides front-line defense against infection as a barrier as well as through immune cells and substances that reside

among the skin cells, helps maintains fluid and body temperature, and contains millions of sensory nerve cells. Most of the body's pain receptors are among these nerve cells. Remarkably resilient and flexible, the skin continually renews itself.

The Nervous System

The nervous system is both command central (the brain) and intercellular highway (the nerves), orchestrating every function within the body—more often than not without conscious awareness of its myriad activities. The nervous system interprets and responds to sensory information, continuously adjusting and accommodating its functions. These functions require chemical messengers—neurotransmitters—as well as electrical activity among cells. Nerves range in size from microscopic to several feet in length.

The Musculoskeletal System

Giving the body the ability to resist the force of gravity to provide shape and mobility is the musculoskeletal system—the bones, connective tissues, and muscles. These structures have density and strength. They use leverage and oppositional function to move the body—walk, run, jump, skip, and even turn cartwheels. These functions require coordination with the nervous system, sensory systems, and balance structures within the inner ear. Health conditions that affect the musculoskeletal system—ranging from injuries such as sprains and fractures to degenerative processes such as osteoarthritis—are among the most common reasons people seek medical care.

Pain and Pain Management

The final section in Volume 1 is "Pain and Pain Management"—not, of course, a body system but rather a discipline (specialty) within the practice of medicine that examines the interactions of the foundational body systems that, when disrupted, result in pain. A complex physiologic experience, pain typically arising from multiple causes that cross these body systems. Consequently, so must its treatment approaches. The entries in "Pain and Pain Management" cover the mechanisms of pain as well as health conditions in which pain is the primary symptom.

THE FACTS ON FILE ENCYCLOPEDIA OF

HEALTH AND MEDICINE

IN FOUR VOLUMES:

VOLUME 1

THE EAR, NOSE, MOUTH, AND THROAT

The structures of the ear, nose, mouth, and throat carry out the functions of hearing, balance, smell, taste, speech, and swallowing. Practitioners in the medical field of otolaryngology specialize in providing care for these structures. This section, "The Ear, Nose, Mouth, and Throat," presents a discussion of the structures and their functions, an overview of otolaryngologic health and disorders, and entries about the health conditions that can affect them.

Structures of the Ear, Nose, Mouth, and Throat

EAR
- outer ear
  - auricle (pinna)
  - auditory canal
- middle ear
  - TYMPANIC MEMBRANE (eardrum)
  - EUSTACHIAN TUBE
- inner ear
  - malleus (hammer)
  - incus (anvil)
  - stapes (stirrup)
  - oval window
  - COCHLEA
  - organ of Corti
  - round window
  - cochlear NERVE
  - bony labyrinth
  - membranous labyrinth
  - semicircular canals
  - vestibule
  - saccule
  - utricle
  - vestibular nerve

NOSE
- nasal cavity
- nasal septum
- nostrils
- mucous lining
- nasal conchae

SINUSES
- frontal
- ethmoid
- sphenoid
- maxillary

- olfactory bulb
- olfactory nerve ending

MOUTH
- lips
- cheeks
- tongue
- taste buds
- palate
- SALIVARY GLANDS
  - parotid
  - submandibular
  - glossopharyngeal
  - lingual
  - sublingual
  - buccal
  - labial

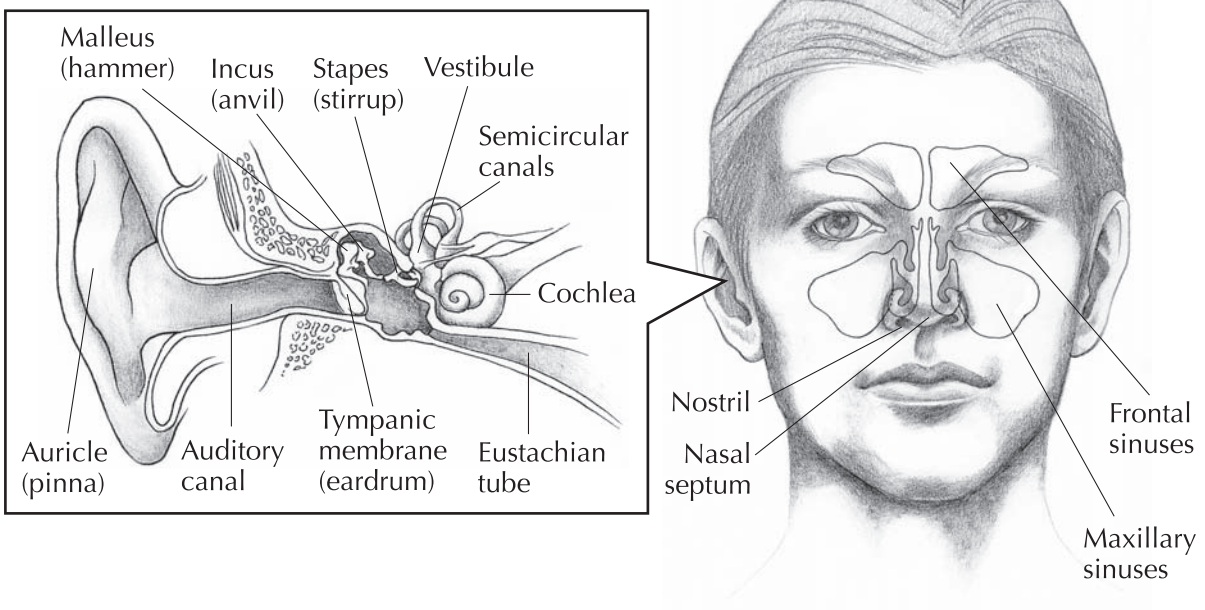
THROAT
- uvula
- pharynx
- epiglottis
- hyoid bone
- larynx
- VOCAL CORDS

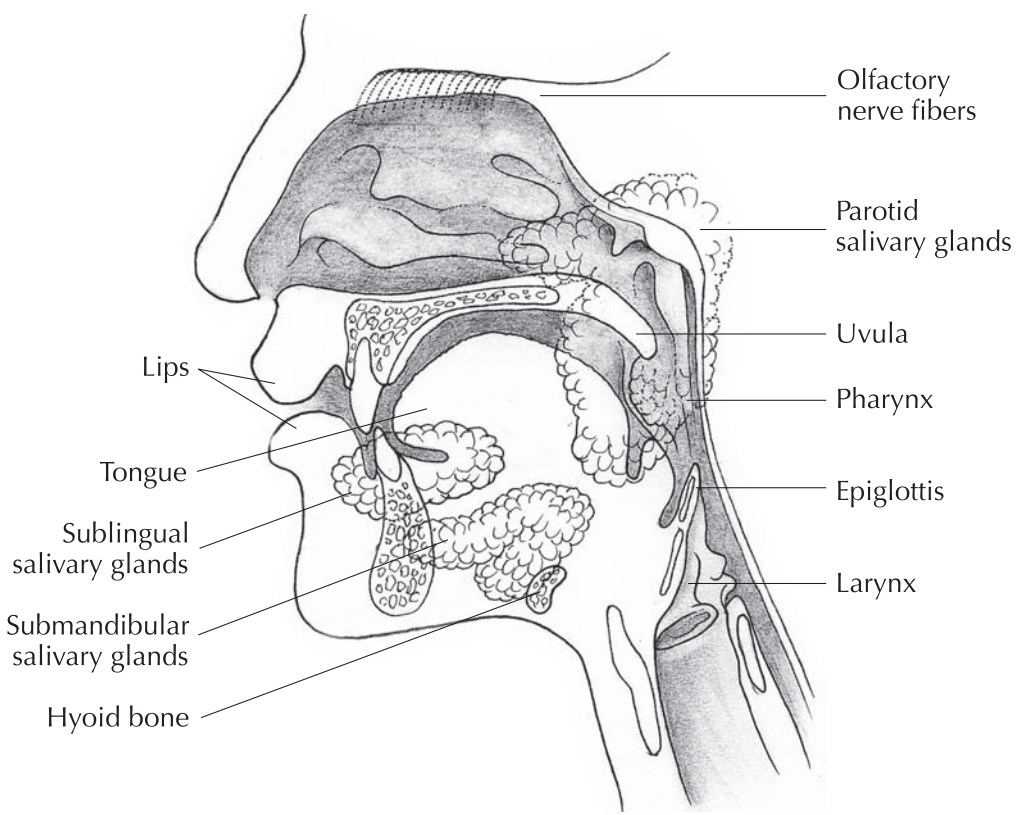
Functions of the Ear, Nose, Mouth, and Throat

The ears, nose, and mouth (along with the eyes) are the primary features of the head and face. They form the hallmarks of recognition and individual identity throughout life. Yet the functions of these features are far more than cosmetic. They are important for survival as well as for refined sensory perception, making it possible to comprehend and interact with the external environment. Taste and smell, the chemosenses, provide the combined sensation of flavor—a blend of the mouth's ability to perceive four distinct tastes and the nose's ability to detect thousands of odors. Hearing allows the BRAIN to register sounds across a broad spectrum of frequency and volume.

The structures responsible for sensory perception begin to take shape as early as the third week of embryonic development and function at a fairly high level by birth. These senses—taste, smell, and hearing—serve as basic survival mechanisms for newborns, helping them identify their mothers, food sources, and hazards until other senses and cognitive abilities adequately develop. Survival also depends on the ability to suck or chew and swallow, requiring coordinated movements of the structures of the mouth and throat. The brain's temporal lobe, which processes hearing, language, and speech as well as smell, takes a developmental leap about three months after a baby's birth, vastly expanding sensory perceptions and communication capabilities. Further cerebral

Structures of the Ear, Nose, Mouth, and Throat





development continues well into ADOLESCENCE, refining the brain's ability to interpret and categorize the signals the senses send to it.

Functions of the ear: hearing and balance Hearing (audition) occurs through air conduction and BONE conduction of sound waves. The structures of the outer and middle ear facilitate air conduction. The outer ear, called the auricle or pinna, is a structure of CARTILAGE and SKIN that extends from the side of the head. Its somewhat dishlike structure serves to "catch" sound waves traveling through the air; its ridges and curves channel those sound waves into the auditory canal. The auditory canal funnels and focuses the sound waves, directing them to the TYMPANIC MEMBRANE or eardrum, which vibrates in response. The tympanic membrane marks the end of the outer ear and the start of the middle ear, creating a sealed chamber. Its vibration activates, in sequence, the three tiny auditory ossicles, or bones, of the middle ear: first the malleus (hammer), then the incus (anvil), and finally the stapes (stirrup). The flat of the stapes rests against the oval window, a small translucent membrane in the wall of the COCHLEA. This point of contact represents the transition from the middle ear to the inner ear and from an environment of air to one of fluid.

The middle ear is pressurized, allowing the tympanic membrane and the auditory ossicles to vibrate freely and without resistance. The EUSTACHIAN TUBE, a short canal of tissue, connects the middle ear with the upper throat at the back of the nose. Somewhat like an elongated valve, it serves to equalize pressure between the middle ear and the external environment. Swallowing and yawning force air into the eustachian tube, causing it to open (sometimes with a perceptible *pop*). Unequal pressure between the middle ear and the atmosphere causes the tympanic membrane to bulge in the direction of the lower pressure, altering its ability to convey the vibrations of sound waves. Circumstances that prevent the eustachian tube from opening to balance air pressure, such as a cold that fills the nasal passages and eustachian tubes with congestion, causes the sensation of muffled hearing and pressure in the ear. When pressure in the middle ear remains lower than the atmospheric pressure for a prolonged time, the body attempts to compensate by drawing fluid into the middle ear. Though the fluid may relieve the sensation of pressure, it further constrains middle ear function. Blocked eustachian tubes establish ideal conditions for middle ear INFECTION (OTITIS media), allowing BACTERIA to move into the middle ear. Until about age 10, the eustachian tubes are nearly horizontal. As the child's facial structure lengthens with maturity the eustachian tubes shift and angle downward from the ears to the throat, improving their ability to drain congestion and remain open.

The vibration of the stapes against the oval window amplifies the energy of the sound waves and sets in motion the fluid (endolymph) within the cochlea on the other side of the oval window. Fluid further focuses and aligns the sound waves into patterns. A second membrane, the round window, dissipates excessive vibration into the fluid of the inner ear (perilymph) on its other side. The moving endolymph within the cochlea in turn stimulates microscopic fibers along a membrane that forms a structure within the cochlea called the organ of Corti. The fibers resonate to specific sound waves, activating NERVE impulses in specialized cells called HAIR cells. The cochlear nerve carries the nerve impulses to the eighth cranial nerve (vestibulocochlear nerve), which in turn transmits them to the brain's temporal lobe. The temporal lobe filters, interprets, and analyzes the nerve impulses, translating them into sound messages including language.

The bony structures of the head and face also conduct sound waves. Bone conduction bypasses the outer and middle ears. Sound waves instead travel as vibrations along the bones to the inner ear, where they pass to the bony part of the cochlea. The vibrations of the bony cochlea pass to the endolymph, and the rest of the hearing process unfolds. Sounds conveyed through bone conduction are significantly restricted in tonal range and volume because they bypass the amplifying structures of the tympanic membrane and auditory ossicles. The sound waves of one's own voice travel primarily through bone conduction along the bones of the face, which explains why it seems so different when heard as a recording in which the sound waves travel by air conduction.

The inner ear also manages the body's balance and motion in relation to gravity. The structures

and functions that do so make up the vestibular system. The bony labyrinth, which also houses the cochlea, supports the membranous labyrinth. Five fluid-filled structures within the membranous labyrinth sense motion and movement: the three semicircular canals, which sense rotational movement, and the saccule and utricle, which sense linear movement. The saccule senses movement that is up-and-down; the utricle senses back-and-forth and left-to-right movement. These structures are all open to one another; however, they form a closed network among themselves that contains endolymph. Movement causes shifts in pressure of the endolymph, which nerve cells register and send as electrical impulses to the vestibular nerve. The vestibular nerve conveys these impulses to the eighth cranial nerve, which in turn carries them to the brain. The brain interprets the vestibular messages along with other input from sensory nerve cells (proprioceptors) located throughout the body, nearly instantaneously responding with neuromuscular signals that initiate movement.

Extremes of movement, such as rapid swinging or spinning, can temporarily disrupt the vestibular system, causing dizziness and NAUSEA. Some people experience such symptoms with less extreme movement, such as riding in a car, boat, or airplane, known commonly as motion sickness. More serious dysfunctions and disorders of the vestibular system, such as MÉNIÈRE'S DISEASE and LABYRINTHITIS, can result in debilitating loss of balance.

Functions of the nose: breathing and smell The nose protrudes from the front of the face. Its placement allows it to draw air into the body in one of life's most basic activities, BREATHING. Most of the nose's external structure is CARTILAGE and SKIN; the nasal bone is less than one half inch long. The ethmoid, vomer, and maxilla bones frame the back of the nose. Ridges in these bones, the nasal conchae, direct the flow of air into the SINUSES. These chambers, along with the nose's mucus lining, moisturize and warm each breath so it does not irritate the airways and lungs. A tissue wall, the nasal septum, divides the nasal cavity into two channels, the nostrils. Tiny hairs line the inner nostrils and are responsible for keeping the nasal passages clear of debris.

The nose is also the body's organ of smell, responsible for the functions of olfaction. The first cranial nerve (olfactory nerve) terminates in the olfactory bulb and a bristlelike patch of olfactory nerve endings along the roof of the nose. These olfactory nerve endings detect the presence of odor molecules in the air that enters the nose. Fibers of the palatine nerves, which detect taste, are also present along the floor of the nose, though not nearly in the abundance with which they infiltrate the mouth. The brain interprets the blend of nerve impulses from the palatine nerve endings and the olfactory nerve endings and integrates them into perceptions of flavor.

Functions of the mouth and throat: taste, swallowing, and speech The mouth and throat make it possible to eat and speak. The powerful masseter muscles open and close the mandible (lower jaw), generating over 500 pounds per square inch of pressure as the TEETH come together to bite and in excess of 3,500 pounds per square inch of force at the back teeth (molars) with chewing. The hyoid bone helps anchor the back of the tongue, another powerful MUSCLE. The SALIVARY GLANDS, present in pairs on each side of the mouth, produce two to three pints of saliva every day. This watery liquid contains enzymes and mixes with food to begin breaking it down, an early stage of digestion, as well as to soften it for swallowing. The cheeks, tongue, and lips help contain food within the mouth and push it to the back of the throat for swallowing; they also shape the flow of air and create the formation of words during speech. These functions require muscular control and coordination.

The sense of taste is called gustation. Though common perception is that the bumps on the tongue are the taste buds, taste buds are microscopic. The bumps are called papillae; they contain clusters of taste buds. Each taste bud contains dozens of taste cells. Though taste buds for the four categories of taste—sweet, sour, salt, and bitter—are present throughout the mouth, the roughly 10,000 of them on the tongue align in patterns of concentration:

- Taste buds on the tip of the tongue are concentrated to detect sweet.

- Taste buds on the sides of the tongue are concentrated to detect sour and salt.
- Taste buds at the back of the tongue are concentrated to detect bitter.

Three CRANIAL NERVES—the 7th (facial), 9th (glossopharyngeal), and 10th (vagus)—carry nerve impulses related to taste to the brain. At its most primitive level, taste helps the brain determine what is safe and what is hazardous to eat. Sweet substances generally contain sugars and carbohydrates, essential nutrients for energy, whereas bitter substances may contain acids or chemicals that are potentially harmful. Recent research indicates that gustation is far more complex than simple delineation among taste buds, however, with some scientists speculating that taste represents learned interpretations as much as response to specific qualities. Further, taste and smell are inextricably intertwined. Though distinct nerve impulses from each reach the brain, the brain analyzes them and creates collective interpretations.

The functions of breathing and swallowing share the structures of the throat. The chamber at the back of the mouth and the top of the throat is the pharynx; it receives both air and food. A flap of cartilage at the base of the pharynx, the epiglottis, closes across the TRACHEA when swallowing and opens to allow the passage of air during inhalation and exhalation. The small flap of tissue that hangs visibly at the back of the throat, the uvula, is an extension of the soft palate. Doctors are uncertain of the uvula's function; it may help keep swallowed food from entering the nasal passages.

The larynx is a sequence of connected cartilage structures that makes speech possible. Air passing through the larynx causes these cartilages and the folds of tissue known as the VOCAL CORDS to vibrate, generating sounds. The muscles of the throat help move the sound vibrations into the mouth, which then forms them into noises and words. Hearing further helps shape speech, providing instant auditory feedback. It is difficult, although not impossible, for someone who has profound HEARING LOSS to speak clearly enough for others to understand. STROKE and neuromuscular disorders such as PARKINSON'S DISEASE are among the common causes of dysfunctions affecting swallowing and speech.

Health and Disorders of the Ears, Nose, Mouth, and Throat

Disorders and dysfunctions of the ears, nose, mouth, and throat range from structural defects present at birth to infections to trauma resulting from ACCIDENTAL INJURIES or diseases such as CANCER. Disturbances of taste, smell, hearing, and balance may accompany numerous health conditions from COLDS to DIABETES, stroke, and Parkinson's disease. Health experts estimate that about 2 million Americans have diminished, altered, or lost functions of taste and smell. More than 28 million have a perceptible loss of hearing ability; 2 million of them are profoundly deaf (unable to hear at a functional level). Disturbances of balance resulting from dysfunctions of the inner ear affect as many as 45 million Americans.

Nearly everyone experiences the most frequent health condition that affects the chemosenses simultaneously: the common cold. Its familiar symptoms include nasal congestion and runny nose (RHINORRHEA), sore throat (PHARYNGITIS), and the sensation of "stuffy" ears and muffled hearing (and sometimes dizziness, when the congestion alters the inner ear's balance mechanisms). This choreography of discomfort results from the intimate integration of both structure and function of these senses.

Limiting or avoiding exposure to loud noise could protect millions of people from hearing loss. Surgical and technological advances hold great promise for restoring some kinds of hearing loss. Though some diminishment occurs naturally with aging, hearing, taste, and smell require minimal effort to maintain healthy function across the spectrum of age.

Traditions in Medical History

Before the advent of ANTIBIOTIC MEDICATIONS and vaccines in the middle of the 20th century, many of today's commonplace ailments involving the ears, nose, mouth, and throat were serious and even life-threatening illnesses. Otitis media (middle ear infection), though less common or perhaps simply less frequently diagnosed 50 years ago than it is

today, accounted for much childhood deafness and frequently led to the complication of MASTOIDITIS, a bacterial infection in the porous mastoid bone behind the ear that in turn often spread to the brain, causing MENINGITIS or ENCEPHALITIS. Even TONSILLITIS frequently resulted in abscesses in children and adults alike; tonsillectomy, in the absence of adequate ANESTHESIA, was not an option.

These infections had grim outlooks, leading to desperate treatments such as lancing (cutting open the ABSCESS or infection) and application of chemical disinfectants (for example, iodine and carbolic acid), which were the standard of treatment for external wounds. The highly toxic nature of these approaches became a calculated risk in the fight for life. Lancing an abscess opened a direct channel into the bloodstream for the BACTERIA, virtually guaranteeing rapid death due to SEPTICEMIA ("blood poisoning" or septic shock). The alternative, however, was suffocation from the swelling that closed off the throat. DIPHTHERIA and PERTUSSIS (whooping COUGH), bacterial infections of the throat, remained the leading causes of childhood death until the 1950s. Today antibiotics, surgery, and routine childhood vaccinations have relegated these diseases, for the most part, to entries in textbooks and encyclopedias.

Breakthrough Research and Treatment Advances

Some the most profound breakthroughs in otolaryngology have been in the area of hearing loss. Digital technology brings the computer to the ear, allowing tiny and fully programmable hearing aids that fit far enough within the auditory canal to be undetectable. Computerized adjustments accommodate individual variations in tonal loss, helping people screen out the kinds of noise interference that have made the traditional HEARING AID a less than ideal solution. The COCHLEAR IMPLANT, which debuted in the 1980s, makes hearing possible for thousands of people with sensorineural hearing loss for whom hearing aids do not work. Hair-thin wires reside within the inner ear, receiving input from outside the ear and conveying it directly to the hair cells within the cochlea in much the same way nerves do. External components collect and, using digital technology, interpret sound signals.

Other advances mark improvements in treatments for ear infections, sinus infections, seasonal allergies, and operations on structures of the orofacial structures. Infants born with cleft deformities today will grow up with little evidence of this once disfiguring CONGENITAL ANOMALY, as advances in anesthesia and surgical techniques now permit surgeons to perform corrective procedures early in childhood and often in a single operation. Endoscopic surgery reduces risk for numerous operations on the nose, middle and inner ear, and throat. New understandings of immune function and allergy response have led to new treatment approaches for chronic SINUSITIS and ALLERGIC RHINITIS. Current research continues to explore age-related changes in hearing, seeking approaches to head off hearing loss.

A

acoustic neuroma A noncancerous tumor of the eighth cranial (vestibulocochlear) NERVE. Acoustic neuromas typically grow over years to decades and in some people cause no symptoms; doctors detect them incidentally. An acoustic neuroma does not invade the surrounding tissues, though it can become life-threatening if it becomes large enough to put pressure on the structures of the brainstem. Most often doctors do not know why acoustic neuromas develop and classify them as idiopathic (of unknown cause). Acoustic neuromas sometimes occur with neurofibromatosis type 2, a rare hereditary disorder in which fibrous growths develop in the CRANIAL NERVES and SPINAL NERVES.

Early symptoms of acoustic neuroma are vague and often perceived as normal consequences of aging because the tumor is so slow growing it typically appears in the later decades of life. Early symptoms include

- gradual loss of hearing, especially difficulty understanding speech, in one EAR
- TINNITUS (rushing or roaring sound) in one ear
- balance disturbances such as dizziness or loss of balance with motion

Advanced symptoms occur when the tumor's size begins to encroach on nearby structures such as the seventh cranial (facial) nerve. Such symptoms might include facial PAIN and disturbances of facial expression. An AUDIOLOGIC ASSESSMENT helps determine the level of HEARING LOSS and whether it affects one or both ears. Hearing loss in both ears suggests causes other than acoustic neuroma; it is very rare that a person would have two tumors, one affecting each vestibulocochlear nerve. MAGNETIC RESONANCE IMAGING (MRI) can usually determine the presence of an acoustic neuroma.

Treatment depends on the extent of symptoms and the person's overall health status. For many people, especially those who have no symptoms, the preferred treatment is watchful waiting (observation and regular tests to monitor the tumor's growth). Surgery to remove the tumor or RADIATION THERAPY to shrink the tumor is an option when symptoms interfere with QUALITY OF LIFE or affect vital brainstem functions such as regulation of BREATHING and HEART RATE or motor control. Each method has risks and benefits; individual health circumstances also influence the decision.

When it exists with no symptoms, acoustic neuroma does not interfere with the regular activities of living or present any threat to health. For most people who experience symptoms and undergo treatment, recovery is complete. Idiopathic acoustic neuromas do not return, though acoustic neuromas associated with neurofibromatosis type 2 often recur. Other than neurofibromatosis type 2, there are no known risk factors or preventive measures for acoustic neuroma.

See also AGING, OTOLARYNGOLOGIC CHANGES THAT OCCUR WITH; CENTRAL NERVOUS SYSTEM; MÉNIÈRE'S DISEASE; SURGERY BENEFIT AND RISK ASSESSMENT; VESTIBULAR NEURONITIS.

adenoid hypertrophy Enlargement of the ADENOIDS, structures of LYMPHOID TISSUE at the back of the NOSE. The purpose of the adenoids is to trap and destroy pathogens (disease-causing agents) in children; by ADOLESCENCE the adenoids atrophy (shrink) and in adults are not distinguishable. When the adenoids swell, they can block the nasal passage. This disrupts BREATHING and can affect the speech. The eustachian tubes open near the adenoids;

swollen and infected adenoids can trap BACTERIA in the EUSTACHIAN TUBE and middle EAR. Adenoid hypertrophy is a leading cause of OTITIS media (middle ear INFECTION) in children.

Symptoms of adenoid hypertrophy include

- frequent ear infections
- MOUTH breathing
- snoring, and, when hypertrophy is severe, OBSTRUCTIVE SLEEP APNEA
- POSTNASAL DRIP
- bad breath (HALITOSIS)

Because the adenoids atrophy with physical maturation, doctors prefer to treat occasional infections with appropriate ANTIBIOTIC MEDICATIONS. ALLERGIC RHINITIS can also cause adenoid hypertrophy. When adenoid infections become chronic or when the swelling does not retreat, doctors may recommend adenoidectomy (surgery to remove the adenoids). Once the adenoids are removed, any related health problems go away.

See also SURGERY BENEFIT AND RISK ASSESSMENT; TONSILLITIS.

aging, otolaryngologic changes that occur with

The natural changes that take place in the structures and functions of the EAR, NOSE, THROAT, and MOUTH as a person grows older. Age-related changes manifest in late childhood, as facial structures elongate, and again in the sixth decade and beyond, as some diminishment of function, particularly sensory perception, develops.

Otolaryngologic Changes in Late Childhood

Though the senses of hearing, taste, and smell are fully developed by about one month of age, changes in facial structure later in childhood alter some aspects of function. The rounded facial structures of the young child begin to change around age five or six and continue into early ADOLESCENCE. The head elongates, expanding the nasal and oral passages. The eustachian tubes lengthen and angle downward, improving their ability to remain patent (open and clear of congestion). The arch of the palate (roof of the mouth) flattens, and the permanent TEETH come in. Control of the tongue, lips, and other muscular structures of the face and neck improves. These changes facilitate the ability to form words. By late childhood, many difficulties with speech begin to resolve. Continued development of the brain's temporal lobe, which processes hearing and language as well as taste and smell, expands and refines speech capabilities and sensory interpretations. Whereas a child may perceive a flavor as "chocolate," an adult will discern that same flavor in terms of multiple descriptors.

Otolaryngologic Changes in Late Life

In healthy adults, sensory perceptions, balance, and language capacity remain intact well into the sixth or seventh decade. Beyond this point, many people experience alterations in taste and smell, and particularly hearing. Health conditions that become more prevalent with age, such as STROKE and PARKINSON'S DISEASE, also affect sensory functions as well as swallowing and speech.

Taste cells, located within taste buds, are the only sensory cells that regenerate, and they do so regularly throughout life. By midlife the rate of regeneration slows, and a person at age 60 has about half as many taste cells as at age 30. The more significant influence on the perception of taste, however, is the loss of olfactory receptors in the nose. The body does not replenish these specialized sensory cells, which detect thousands of odors in comparison to the four basic qualities the sense of taste detects. By age 70 there are about a third as many olfactory receptors as at age 30. These changes influence a person's interest in food and desire to eat, which commonly becomes a reason for inadequate nutrition and diet in the elderly. As well, the loss of teeth due to DENTAL CARIES (cavities) and gum diseases such as PERIODONTAL DISEASE, and decreased saliva production, diminish the ability to chew, further restricting food choices.

The clinical term for age-related HEARING LOSS is PRESBYCUSIS. The HAIR cells within the COCHLEA, which respond to the frequencies of the vibrations that pass into the inner EAR, are extraordinarily sensitive. By the sixth or seventh decade of life, the fibers of the hair cells, particularly those sensitive to high frequency vibrations, break and experience other damage. This causes loss of the ability to register sounds in those frequencies, which manifests as hearing loss. As these are the fre-

quencies of normal conversation, the loss, though gradual, becomes apparent. Hearing aids that amplify sound waves in these frequencies can help restore the function of hearing. OTOSCLEROSIS (fusion of the auditory ossicles, the tiny bones of the inner ear) and damage to tissues that results from impaired blood circulation (caused by ATHEROSCLEROSIS, for example) also diminish hearing.

See also BRAIN; EUSTACHIAN TUBE; GENERATIONAL HEALTH-CARE PERSPECTIVES; NUTRITIONAL ASSESSMENT; SPEECH DISORDERS; SWALLOWING DISORDERS.

audiologic assessment Tests to measure hearing ability and to determine the extent of HEARING LOSS. An audiologic assessment consists of preliminary screening and procedures to test specific dimensions of hearing. A comprehensive audiologic assessment may take up to an hour to complete though requires no preparation and involves no discomfort. Basic screening for hearing ability and loss should begin in infancy (90 percent of newborns born in hospitals in the United States are tested before discharge or at the first newborn well-care visit) and continue through life. Health experts recommend routine screening tests for hearing loss in adults every five years, more frequently when there are risk factors, such as noise exposure.

Preliminary Examination

The first step in an audiologic assessment is a preliminary examination in which the audiologist examines the structures of the outer and middle ears with an otoscope. This examination, called an OTOSCOPY, helps detect structural anomalies as well as mechanical impediments to sound conduction (such as compacted CERUMEN in the auditory canal or an infected or damaged TYMPANIC MEMBRANE). The preliminary examination also includes a health history in which the audiologist asks questions about any existing hearing loss, risk factors for hearing loss (including noise exposure), medications, and illnesses such as MEASLES and RUBELLA (German measles).

Audiometry

An audiologist conducts the procedures of audiometry, a battery of tests that measure the ability to discern sounds at different frequencies (pitch) and intensities (volume). During the audiometric examination the person sits in a soundproof booth and the audiologist sits in a control booth. Common audiometric procedures include

- Pure-tone audiometry, which measures the range of sound a person can hear. For this procedure, the audiologist produces tones at certain frequencies and intensities, and the person indicates whether he or she hears them. The audiologist tests each EAR separately.
- Conditioned-play audiometry and visual-reinforcement audiometry, which adapt conventional audiometry to children. These methods use games and visual rewards to elicit responses to the tones.
- Speech audiometry, which determines the lowest sound frequency and intensity at which a person can hear and repeat two-syllable spoken words (speech-reception threshold), and how well the person can hear and repeat single-syllable words spoken at a consistent intensity (word recognition).
- Pure-tone BONE-conduction audiometry, which delivers tones through a vibrating device placed against the bone near the ear. This bypasses the outer and middle ear when there are conductive obstructions present (such as OTITIS media or compacted cerumen in the auditory canal).

The audiologist reports results in decibel (dB) of threshold (sound intensity) for 500 Hertz (Hz), 1,000 Hz, and 2,000 Hz, the frequencies of everyday speech and activities. An audiogram summarizes and presents this information for each ear in a graphic presentation. Any identified hearing loss may require additional tests.

Other Hearing Tests

Sometimes health-care providers need further information to identify the nature and cause of hearing loss, particularly in infants and young children. Other tests for refined assessment include

- auditory evoked potentials, in which electrodes attached to the head measure NERVE transmissions in response to sound
- auditory brainstem response, an auditory evoked potential that specifically measures the response of the eighth cranial nerve (vestibulocochlear or auditory nerve)

- otoacoustic emissions, which measure the response of the cochlea to sound stimulation
- acoustic immittance measures, which assess the function of the middle ear:
  - † tympanometry, to assess eardrum function
  - † acoustic reflex, to determine whether the ear responds to loud sounds
  - † static acoustic impedance, to measure volume of air within the ear canal
- balance assessment to determine vestibular function/dysfunction

Understanding Results

Audiologic assessment helps determine the appropriate therapeutic course for hearing loss. Doctors often can correct conductive hearing loss through medical or surgical interventions. Sensorineural hearing loss requires hearing aids or other solutions (such as a COCHLEAR IMPLANT) to improve hearing ability. Mild hearing loss (26 to 30 dB) is the point at which a person is likely to benefit from a HEARING AID. At the level of severe hearing loss (71 to 90 dB), a person is unable to understand speech without a hearing aid. Because hearing is essential for development of language and communication skills, it is especially important to provide immediate intervention for hearing loss in children.

See also AGING, OTOLARYNGOLOGIC CHANGES THAT OCCUR WITH; NOISE EXPOSURE AND HEARING; OTOSCLEROSIS; OTOTOXICITY.

B

barotrauma Damage to the structures of the EAR resulting from the ear's inability to equalize pressure with abrupt and extreme changes in atmospheric pressure. Such changes most often occur in situations of sudden altitude change such as air travel or diving, though also may result from a sharp blow to the ear that forces a blast of air into the auditory canal. Any of the three parts of the ear—outer, middle, and inner—can experience injury from barotrauma.

- Outer ear barotrauma typically takes the form of small, painful blisters and hemorrhages along the walls of the auditory canal.
- Middle ear barotrauma commonly includes a ruptured TYMPANIC MEMBRANE (eardrum). The pressure within the middle ear can become intense before the tympanic membrane gives way, causing much PAIN. With rupture the pressure immediately equalizes, though hearing ability temporarily diminishes.
- Inner ear barotrauma causes sudden and usually significant VERTIGO (extreme dizziness and balance disturbances) and HEARING LOSS that can be permanent.

Most outer and middle ear barotrauma heals on its own. Many ruptured eardrums heal naturally, though large or irregular tears require surgical repair (TYMPANOPLASTY). Inner ear barotrauma may require surgery to repair damaged structures and may result in permanent functional loss if the damage is extensive.

Preventive measures to reduce the likelihood of barotrauma include chewing gum, frequent swallowing, and yawning during activities that involve changes in barometric pressure such as descending during air travel. Some people benefit from nasal decongestant sprays that clear the nasal passages and eustachian tubes. Recreational divers are at greatest risk for inner ear barotrauma; pressure changes are most drastic nearer the surface than deep in the water.

See also BLISTER; EUSTACHIAN TUBE; HEMORRHAGE.

benign paroxysmal positional vertigo (BPPV) A disorder of the inner EAR in which certain positions of the head cause sudden and severe, though brief, episodes of VERTIGO (sensations of spinning or motion). Many people experience symptoms upon awakening from sleep, as they roll from one position to another or tilt their heads. Though the vertigo episode typically lasts only a few minutes, it can result in feelings of NAUSEA and dizziness as well as balance disturbances, that continue for several hours.

Doctors believe calcifications called otoconia, small "stones" of calcium carbonate, cause BPPV. Otoconia occur naturally in the utricle and saccule, two of the structures within the inner ear that are part of the vestibular system, the body's balance mechanisms. When otoconia escape from the utricle they can enter the semicircular canals, where they collide with NERVE endings that send positional messages to the BRAIN. These collisions overwhelm the messaging network. The otoconia tend to dissolve in the inner ear fluid over time. About half the people who develop BPPV experience head trauma or serious INFECTION, such as OTITIS (ear infection) or SINUSITIS (sinus infection), before BPPV symptoms begin, leading doctors to believe that such assaults on the integrity of the inner ear jars the otoconia out of the utricle.

Symptoms and Diagnostic Path

The key symptom of BPPV is sudden, severe, and limited episodes of vertigo without TINNITUS (ringing or rushing sound in the ears) or hearing impairment. The presence of either or both of the latter suggests another disorder. Symptoms tend to occur with certain positions, though symptoms can occur even when avoiding trigger positions. Between episodes, there are no symptoms. The pattern of symptoms is fairly conclusive, though doctors typically conduct a comprehensive AUDIOLOGIC ASSESSMENT to determine whether there is any HEARING LOSS with the expectation that results will be normal.

Other diagnostic procedures for BPPV may include

- Dix-Hallpike test, positional test performed during physical examination; positive for BPPV when it causes NYSTAGMUS (rapid and involuntary darting movements of the eyes) or brings on an episode of vertigo
- caloric test, in which the doctor gently instills warm and then cold water into each ear; normal response evokes vertigo and abnormal response, diagnostic of BBPV, evokes little or no vertigo
- electronystagmography, in which tiny electrodes placed around the eyes detect the abnormal darting eye movements characteristic of vertigo
- imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to rule out other possible causes for the symptoms

The combination of test results and history of symptoms helps the doctor distinguish BPPV from other disorders that affect the vestibular system.

Treatment Options and Outlook

For many people who have BPPV, the symptoms simply go away over time, generally within several months, as the inner ear fluid dissolves the otoconia. Some people benefit from ANTIHISTAMINE MEDICATIONS or scopolamine, drugs that suppress vestibular function, or antinausea medications. There are several positional treatments (among the most commonly used are the Epley maneuver and the Semont maneuver) that some doctors perform to attempt to jolt the otoconia out of the semicircular canals and at least into the vestibule if not back into the utricle. These maneuvers succeed 70 to 90 percent of the time.

Rarely the otolaryngologist may recommend one of two operations for BPPV if it continues for longer than a year without response to other treatment:

- Posterior ampullar neurectomy severs a branch of the nerve that conveys motion signals from the utricle, ending its ability to send messages of motion to the brain.
- Posterior canal plugging seals the involved semicircular canal so the otoconia can no longer float in its fluid.

Surgery nearly always ends BPPV; when it does not, further examination typically reveals complicating factors or conditions that contribute to the symptoms. Nearly everyone who develops BPPV eventually recovers fully from the condition, with balance restored to normal. During the course of the condition and while undergoing treatment with one of the maneuvers, doctors recommend avoiding positions that may trigger symptoms, especially tilting the head back, until BPPV symptoms no longer occur. Once BPPV is resolved, it generally does not recur.

Risk Factors and Preventive Measures

Otoconia seem to naturally occur in many people, causing problems only when they become lodged in vestibular structures such that they interfere with the movement of fluid that is essential for balance. It also appears that the body's natural processes dissolve and absorb the otoconia over time, so most of these calcifications do not become large enough to obstruct the vestibular channels. Because doctors do not know what causes otoconia to form, there are no known methods for preventing them. Prompt treatment for ear and sinus infections to reduce further trauma to the inner ear may help keep otoconia from causing symptoms.

See also ACOUSTIC NEUROMA; MÉNIÈRE'S DISEASE; OPERATION; SURGERY BENEFIT AND RISK ASSESSMENT; VESTIBULAR NEURONITIS.

blowing the nose The process of clearing mucus and congestion from the nasal passages. Blowing

the NOSE generates significant pressure that can force congestion into the SINUSES and eustachian tubes. The best method is to blow through both nostrils with a gentle and steady pressure with the head upright, pausing between blows to allow gravity to help move congestion downward toward the nostrils. Short, hard bursts of blowing can activate a REFLEX action, which commonly occurs after a SNEEZE, in which the nasal passages briefly swell and fill with mucus. Doctors believe this reflex congestion occurs as a protective measure to block harmful substances from entering the nose, as sneezing is a mechanism for ejecting foreign matter from the nose. Applying unscented lotion or aloe to the SKIN around the nostrils helps protect against irritation and INFLAMMATION from frequent nose blowing.

See also COLDS; EPISTAXIS; EUSTACHIAN TUBE; FOREIGN OBJECTS IN THE EAR OR NOSE; NASAL VESTIBULITIS; POSTNASAL DRIP; RHINORRHEA; SINUSITIS.

Bogart-Bacall syndrome An overuse condition affecting the VOCAL CORDS and larynx. The key characteristic is a low, husky speaking voice (such as immortalized by famed actors Humphrey Bogart and Lauren Bacall, the namesakes of this condition). Speaking in the lower registers of pitch strains the muscles of the larynx and the tissues of the vocal cords, causing symptoms such as voice fatigue (inability to maintain volume when speaking), soreness or PAIN in the THROAT, and hoarseness or raspiness when speaking. Treatment focuses on improving breath control to speak when the lungs contain an adequate volume of air. Efficient BREATHING during speech lessens the tension of the muscles in the throat that control the vocal cords and flow of air. Some people, particularly women, whose voices are naturally in a higher register of pitch than the voices of men, benefit from VOICE THERAPY to learn to speak at a higher pitch.

See also LARYNGITIS; PHARYNGITIS; SPEECH DISORDERS; SWALLING DISORDERS; VOCAL CORD NODULE; VOCAL CORD POLYP.

broken nose A FRACTURE of the nasal BONE, typically resulting from a direct blow. The NOSE is especially vulnerable to impact injuries, and the nasal bones are the most commonly fractured on the face. Injury to the CARTILAGE and other tissues of the nose often accompanies a nasal fracture; these injuries are typically painful and result in significant swelling and bruising. A fracture can displace the bones and the cartilage, altering the flow of air through the nose, and can result in bleeding within the nasal passages. Ice applied to the area as soon as possible after the injury helps contain the swelling.

Most often the doctor will order X-rays of the face to confirm a nasal fracture as well as to determine whether other fractures, such as of the orbital bones around the eyes, also exist. The doctor often can reduce (reposition) a simple nasal fracture by external manipulation done with local ANESTHESIA (closed reduction). Injury more extensive than a simple nasal fracture typically requires surgery to return the bones to their normal positions (open reduction). A protective splint worn over the nose helps safeguard the fracture from further injury while it heals. The bones become set in about a week; the fracture heals fully in four to six weeks. Sometimes after HEALING is complete the structures of the nose remain out of alignment, which can affect BREATHING. Such complications require further medical assessment by an otolaryngologist or facial surgeon and may require further surgery. Most nasal fractures heal uneventfully and have no long-term consequences.

See also RHINOPLASTY; SEPTAL DEVIATION; SURGERY BENEFIT AND RISK ASSESSMENT; X-RAY.

C

canker sore Ulcerous sores, also called aphthous ulcers, that develop inside the MOUTH. The typical canker sore is round, with a slightly white center and a red rim. Sometimes a tingling or burning sensation precedes the eruption of the sore. A canker sore is painful and irritating for three to five days, then begins to heal and generally goes away in about three weeks. Researchers do not know what causes canker sores, though the tendency to develop canker sores appears to run in families. Theories about the causes of canker sores include immune function abnormalities, nutritional deficiencies, and FOOD ALLERGIES. Some women notice canker sores are more common when they are menstruating.

Treatment targets relieving the discomfort and may include

- frequently rinsing the mouth with a weak solution of saltwater, hydrogen peroxide, diphenhydramine liquid, or milk of magnesia (rinse and spit, do not swallow any of these solutions)
- applying milk of magnesia or a topical anesthetic preparation for oral use directly to the canker sore with a cotton swab
- taking acetaminophen or a nonsteroidal anti-inflammatory DRUG (NSAID) for generalized pain relief
- taking a lysine supplement
- avoiding foods and seasonings that irritate the canker sores

Prescription medications containing amlexanox (such as the brand-name product Aphthasol) may reduce INFLAMMATION and expedite HEALING when sores are large or occur frequently. Such medications come in topical and mouthrinse preparations. Researchers have yet to identify any preventive measures to keep canker sores from developing.

See also COLD SORE; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); NUTRITIONAL NEEDS.

cauliflower ear A casual and descriptive term for an auricle (external EAR) damaged and deformed through trauma. Cauliflower ear is commonly associated with repeated injury such as occurs with boxing. However, even a single blow to the ear significant enough to cause bleeding can result in deformity as the cartilaginous structure of the external ear heals. CARTILAGE has no BLOOD supply of its own but instead draws nutrients from the blood supply of the SKIN. Any damage that disrupts blood flow (such as injury that causes bleeding) causes cartilage tissue to die. Where cartilage dies, the structure it supports shrinks as the skin around it heals, forming the characteristic irregularities of cauliflower ear.

Prompt treatment of any injury to the external ear to minimize the interruption of blood flow and control any INFECTION that may develop helps prevent deformity. Ear PIERCINGS into the upper ear that become repeatedly infected or cause scarring also can result in cauliflower ear. OTOPLASTY (surgery to alter the appearance of the auricle) can improve the auricle's appearance though may not be able to restore it to its natural structure. A key preventive measure is wearing appropriate headgear during activities that expose the outer ears to the risk of traumatic injury.

See also ATHLETIC INJURIES; BLEEDING CONTROL; LACERATIONS.

cerumen A soft waxy secretion, commonly called EAR wax, that the glands in the auditory (ear) canal produce to help remove debris from

within the canal. Cerumen is usually yellowish brown in color and its presence is normal, though many people attempt to clean it from the ears for aesthetic reasons. Most health experts recommend against using cotton swabs within the auditory canal for this purpose; it is possible for the swab to compact the cerumen, push foreign objects deeper into the ear, or damage the TYMPANIC MEMBRANE (eardrum). Tightly compacted cerumen can block sound waves from traveling through the auditory canal, interfering with hearing, and create unequal pressure, causing balance disturbances. It also can trap water in the auditory canal, allowing fungal or bacterial INFECTION to develop. Softening drops help loosen compacted cerumen so the ear's natural mechanisms can push it out of the auditory canal. When this does not work, removal may require a health-care provider to perform EAR LAVAGE or other techniques.

For further discussion of cerumen within the context of otolaryngologic structure and function, please see the overview section "The Ear, Nose, Mouth, and Throat."

See also CLEANING THE EAR; FOREIGN OBJECTS IN THE EAR OR NOSE.

cholesteatoma A growth that develops within the middle EAR. Most cholesteatomas develop as a consequence of frequent middle ear infections (OTITIS media) or chronically blocked eustachian tubes, such as by frequent SINUSITIS (sinus infection) or ALLERGIC RHINITIS. A cholesteatoma starts as an outpouching of SKIN on or near the TYMPANIC MEMBRANE (eardrum). SKIN cells accumulate inside the pouch, causing it to enlarge and exert pressure against the tympanic membrane and auditory ossicles (tiny bones of the middle ear). Over time the increased pressure can destroy the auditory ossicles, causing HEARING LOSS. A large cholesteatoma can also exert pressure inward against the inner ear, causing VERTIGO and balance disturbances.

Symptoms of cholesteatoma include the sensation of fullness in the affected ear, diminished hearing, dizziness and vertigo if there is pressure against the inner ear, and aching or dull PAIN behind the ear. Symptoms are often positional and may worsen at night, especially pain. Some people experience a puslike drainage, often apparent on the pillow. The diagnostic path may include X-rays, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI) of the head. Treatment requires overcoming any INFECTION with ANTIBIOTIC MEDICATIONS and sometimes surgery to remove the cholesteatoma and clean the area.

Treatment often restores hearing, though when the cholesteatoma is large or has been present for a long time the otolaryngologist may be unable to repair the damage to the middle ear. Damage that occurs within the inner ear often is permanent. Prompt treatment of sinusitis or otitis minimizes the risk for cholesteatomas to develop, though these growths are not preventable. Early diagnosis and treatment of cholesteatoma offers the best opportunity to prevent permanent hearing loss and vestibular (inner ear) dysfunction. Untreated cholesteatoma can result in profound hearing loss in the affected ear as well as MASTOIDITIS and MENINGITIS.

See also ACOUSTIC NEUROMA; TYMPANOPLASTY; X-RAY.

cleaning the ear Hygienic measures to keep the ears clear of debris. For the most part, the ears are self-cleaning. Tiny hairs (cilia) line the inside of the auditory canal, moving in wavelike motions to sweep particles of dust and pollen, as well as sloughed SKIN cells, to the outer edge of the EAR. CERUMEN, or ear wax, helps collect these particles for easy removal. Most people need only to wash the outer ear during regular bathing to remove any accumulations of cerumen and debris. However, many people feel the need to wipe the inside of the auditory canal with cotton swabs. Most health-care providers recommend against this. Persistent swabbing of the auditory canal can lead to compacted or impacted cerumen that blocks the canal, interfering with hearing as well as preventing the ear's normal cleansing mechanisms from functioning. It also is possible for pieces of the cotton swabbing to come off inside the canal, creating obstructions, and to perforate the TYMPANIC MEMBRANE with the tip of the swab. A doctor should evaluate any concerns about excess cerumen or foreign objects in the ear. A health-care provider can perform EAR LAVAGE when additional cleaning is necessary. A popular admonition among otolaryngologists is, "Never put anything smaller than an elbow into the ear."

See also FOREIGN OBJECTS IN THE EAR OR NOSE.

cleft palate/cleft palate and lip Congenital anomalies in which the bones of the face that form the roof of the MOUTH fail to close properly in the early stages of embryonic development. These structures originate as separate entities and, in the course of normal embryonic development, join together by 10 weeks of gestation. Cleft defects, known clinically as congenital craniofacial anomalies, occur in varying degrees and combinations that may include separations of the hard palate, soft palate, upper gum, and upper lip. The most common presentation is isolated cleft palate (the defect involves only the roof of the mouth), or cleft palate and lip (the defect extends from the roof of the mouth to the external lip). These anomalies are the fourth most common type of birth defect in the United States, affecting about 1 in 1,000 infants born each year.

An intact palate is necessary for proper eating, swallowing, and speech. An infant with a cleft palate, and especially cleft palate and lip combination, often cannot suck well enough to obtain adequate nutrition. A complete cleft palate blends the nasal and oral openings into a single chamber, which interferes with BREATHING. Craniofacial anomalies also occur among the deformities of numerous other congenital syndromes. There is a particular correlation between isolated cleft palate and other congenital defects, notably HEART anomalies. Because of these correlations, doctors evaluate newborns with cleft palate defects for other congenital disorders.

Symptoms and Diagnostic Path

Doctors detect most cleft palate defects shortly after birth or in early childhood. Many clefts are visible or palpable (the doctor can feel the defect by running a finger along the roof of the infant's mouth). A missing or bifid (two-part) uvula, the small flap of tissue that hangs from the soft palate at the back of the THROAT, often though not always indicates a cleft palate. Doctors may not detect minor cleft palate disorders until the infant has trouble eating or does not appear to be gaining weight. X-rays, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI) are among the procedures that can confirm and define the extent of the defect.

Treatment Options and Outlook

Nearly always surgery is the treatment of choice to close the cleft, for functional as well as aesthetic reasons. Surgeons generally prefer to do these operations as early as the infant's health permits, typically between the ages of 3 and 18 months. Mild to moderate defects often require only a single operation. Extensive deformities may require two or three operations done in stages, with follow-up speech therapy. Severe deformities that involve the upper gum and structure of the TEETH may require ongoing orthodontic and dental work, along with speech therapy, extending into ADOLESCENCE. The outlook following surgical repair is exceptional, with few complications for most infants as they grow older. By adulthood there generally is little apparent evidence of the cleft or its repair.

Risk Factors and Preventive Measures

Cleft palate and cleft lip appear to be random occurrences though are common with certain genetic disorders such as DOWN SYNDROME. Some studies suggest that these disorders are more common among infants of mothers who take certain antiseizure medications or ANTIANXIETY MEDICATIONS in the benzodiazepine family. Cleft palate and cleft lip are also more frequent among children of women who drink ALCOHOL and smoke cigarettes before and during pregnancy. Other studies show that taking folic acid and vitamin B supplements during pregnancy, which is a standard practice in PRENATAL CARE in the United States to reduce the likelihood of NEURAL TUBE DEFECTS, helps prevent craniofacial clefts. When a woman gives birth to a child who has a cleft palate, any subsequent children are more likely than normal to have the same kind of disorder.

See also CONGENITAL ANOMALY, CONGENITAL HEART DISEASE; FETAL ALCOHOL SYNDROME; OPERATION; SMOKING AND HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT; SWALLOWING DISORDERS; VACTERL; X-RAY.

cochlea The organ of the inner EAR that converts sound waves to NERVE impulses. Contained within the bony labyrinth, the cochlea resembles a snail shell. Thousands of specialized nerves, called HAIR cells because of the fine fibers that project from

them, line the fluid-filled inner chamber of the cochlea. The membrane that contains the hair cells is the organ of Corti. Sound waves activate the hair cells, which convert the stimulation into nerve signals. The nerve signals converge at the cochlear nerve, which carries them to the vestibulocochlear nerve (eighth cranial nerve) for transport to the BRAIN. The hair cells are very sensitive and vulnerable to damage from excessive noise. The longest of the hair cells are those that respond to sounds in the decibel range of normal speech; because of their length, they are the most vulnerable to such damage. Hair cells also break off with aging. Damaged cochlear hair cells do not regenerate.

For further discussion of the cochlea within the context of otolaryngologic structure and function, please see the overview section "The Ear, Nose, Mouth, and Throat."

See also AGING, OTOLARYNGOLOGIC CHANGES THAT OCCUR WITH; COCHLEAR IMPLANT; CRANIAL NERVES; HEARING LOSS; PRESBYCUSIS.

cochlear implant An inner EAR prosthesis to provide a degree of hearing ability for those who have profound HEARING LOSS—greater than a 90 decibel (dB) loss of hearing—in both ears and receive no benefit from hearing aids. This tiny electronic device receives incoming sound waves and translates them into frequency impulses that stimulate undamaged auditory nerve fibers that remain within the COCHLEA. The NERVE fibers convey the impulses to the BRAIN via the cochlear nerve. Though there are several designs of cochlear implant, all feature external components and internally implanted electrodes.

Because the nerve fibers within the cochlea are limited the impulses those fibers convey to the brain are also limited, leaving "gaps" in speech. Over time, the person learns where these gaps are and learns to interpret many of them into intelligible units of language. It can take adults several years to develop proficient hearing skills. The level of restored hearing generally correlates to the length of time between the onset of profound hearing loss and placement of the cochlear implant. Children who receive cochlear implants typically learn or regain language understanding and speech skills more quickly than adults, though children who have been profoundly deaf since birth (prelingual loss of hearing) typically do not acquire hearing and speaking skills comparable to those of children who have normal hearing.

See also AUDIOLOGIC ASSESSMENT; SIGN LANGUAGE.

cold sore An eruption of the HERPES SIMPLEX virus 1 (HSV1) in the form of a sore with a crusty scab, most commonly on the lips. Less commonly HSV2, the variation of the herpes simplex VIRUS that causes GENITAL HERPES, causes sores around the MOUTH. Which variation of the herpes virus that is responsible does not matter. People sometimes refer to cold sores as FEVER blisters because they tend to appear with fever or during viral infections such as COLDS; doctors believe viral infections are among the triggers that activate HSV1. Hormonal shifts during MENSTRUATION and exposure to the sun also appear to activate HSV1.

HSV1 lies dormant in the nerve endings in the SKIN near the sites where cold sores have previously occurred and, when activated, causes new sores to erupt. Many people experience itching or tingling at the site in the 24 to 36 hours before a cold sore erupts. Doctors call this the prodrome stage. When sores are present the herpes virus is highly contagious and easily spread to other body locations as well as to other people through contact or shared items such as drinking glasses, straws, and eating utensils. Rubbing the EYE after finger contact with a cold sore can spread the virus to the eye, where it can infect the CORNEA and cause scarring that can lead to blindness. Frequent HAND WASHING is an effective method for restricting the spread of the virus.

Treatment options are limited. Doctors may prescribe ANTIVIRAL MEDICATIONS for recurrent or severe episodes of cold sores. These medications appear to shorten the course of the INFECTION from the usual 7 to 10 days to 3 to 5 days when taken or applied at the first indication (ideally in the prodrome stage) of activation. Numerous topical products to provide relief and moisturization are available over the counter, though these preparations do not shorten the course of the infection. Some people have fewer cold sores when they take lysine supplements. Cold sores typically heal without scarring or other complications.

See also CANKER SORE; CORNEAL INJURY; OCULAR HERPES SIMPLEX.

cough The forceful expulsion of air through the airway as a REFLEX designed to prevent matter, including mucus, from entering the LUNGS. Cough can be a symptom of many health conditions, from minor and temporary irritations of the pharynx (upper THROAT) and structures of the airways, such as those COLDS and allergens can cause, to serious and potentially life-threatening conditions such as laryngeal CANCER, TUBERCULOSIS, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), and LUNG CANCER. Cough also can signal a blockage of the airway, which is a medical emergency. Occasionally cough is an undesired SIDE EFFECT of certain medications, notably the angiotensin-converting enzyme (ACE) inhibitor medications prescribed to treat HYPERTENSION (high BLOOD PRESSURE).

Coughs fall into two major classifications: acute and chronic. Acute cough comes on suddenly and lasts less than three weeks; chronic cough continues for longer than three weeks. Within these classifications, cough may be productive (bring up mucus or sputum) or nonproductive (typically a dry, hacking cough). Treatment depends on the kind of cough and focuses on first eliminating any underlying causes. There are two main classifications of cough medications: antitussive (suppresses the cough) and expectorant (thins the mucus).

When Cough Is an Emergency

A sudden cough, especially one that comes on when eating, may indicate that the person has aspirated (inhaled into the airway) a particle of food or other object. Do not allow someone who starts coughing while eating to leave the table unattended. Instead, ask the person to give a verbal answer to the question, "Are you okay?" If the person cannot speak to answer the question, he or she likely has a blocked airway.

Aspiration is a medical emergency that requires prompt response. Perform a HEIMLICH MANEUVER immediately for a blocked airway. Call 911 for emergency medical aid if the coughing or choking continues.

Acute Cough

An acute cough generally accompanies a health condition of sudden onset such as an upper respiratory INFECTION (colds, flu, BRONCHITIS, PNEUMONIA), SINUSITIS (sinus infection), and PHARYNGITIS. An acute cough can be either productive or nonproductive though is usually productive because the IMMUNE SYSTEM increases mucus production to help rid the body of the PATHOGEN. ANTIBIOTIC MEDICATIONS are necessary to treat infections that are bacterial. Viral infections typically run their course and do not require medications except to relieve symptoms. In infections, coughs are often productive, bringing up dead cells and other debris that the body needs to clear from the airways. POSTNASAL DRIP, which irritates the pharynx, is a key cause of coughs related to upper respiratory infections.

COVERING A COUGH

Coughs can spread infections both through droplets in the air and through hand contact. Health experts recommend coughing into the crook of the arm rather covering the mouth with the hands. Frequent HAND WASHING also helps reduce the spread of pathogens.

Chronic Cough

A chronic cough may signal an underlying health condition or may exist as a response to continued irritation, most commonly cigarette smoking. Other common causes of chronic cough include

- GASTROESOPHAGEAL REFLUX DISORDER (GERD), in which gastric acid from the stomach enters and irritates the throat
- asthma and seasonal allergies
- chronic sinusitis
- pulmonary diseases such as chronic bronchitis, COPD, and BRONCHIECTASIS

Generally, eliminating the underlying cause of chronic cough also eliminates the cough. A significant risk with smoker's cough is that it develops so gradually the smoker may not realize how often he or she coughs. The cough may exist as a response to the irritation of smoking or may signal a serious health condition such as lung disease or

throat or lung cancer. A doctor should evaluate chronic cough in smokers on a regular basis to monitor for more significant health problems. SMOKING CESSATION may end the cough; cough that continues longer than six months beyond smoking cessation may indicate another health condition and requires a doctor's assessment.

Treating Cough

Treatment focuses first on eliminating any underlying reasons for cough. Antibiotic medications are helpful only when there is a bacterial infection. The most effective cough suppressant medications are those which contain DEXTROMETHORPHAN, benzonatate, or NARCOTICS such as codeine and hydrocodone. Products containing benzonatate (a non-narcotic) or narcotics require a doctor's prescription and are not generally appropriate for chronic cough. Products containing dextromethorphan are numerous and available over the counter; extended-release products can provide relief for 10 to 12 hours per DOSE.

Expectorants help thin mucus and secretions so the coughing mechanism can more easily bring them out of the airways. Doctors do not agree on whether expectorants are truly helpful, and there are few clinical research studies that have investigated their effectiveness. The most common expectorant in cough products sold in the United States is guaifenesin. Manufacturers recommend drinking plenty of water when taking products containing guaifenesin; some health experts believe increased water intake alone is adequate to thin mucus.

Most cough products, both prescription and over the counter, combine ingredients, so it is important to read product labels carefully. Products may include a cough suppressant and an expectorant as well as a decongestant, an antihistamine, and other substances. Maintaining adequate moisture in the air (as with a cool humidifier), drinking plenty of liquids, and avoiding substances that irritate the throat and airways are effective nonmedication methods for managing cough, especially chronic cough.

See also ALLERGIC RHINITIS; ALLERGY; PERTUSSIS; PULMONARY EMBOLISM; SMOKING AND HEALTH.

croup A viral INFECTION of the upper respiratory tract that produces a characteristic barking COUGH, most commonly in children under age three. Other symptoms include rapid BREATHING, a high-pitched noise with inhalation (stridor), and FEVER. In many children, the top of the airway at the back of the THROAT becomes swollen and congested, reducing the flow of air. The barking cough results from air being forced through this narrowed passage as the body attempts to clear the congestion of the infection. Croup often follows COLDS and its symptoms tend to worsen at night. The most effective treatment is prompt exposure to moist air. Parents often find that as soon as they get the child buckled into the car seat for the late-night trip to the hospital emergency room, coughing lessens and breathing eases. The cool night air helps open the airways. Often it brings the child relief to sit, wrapped in a blanket for warmth, with a parent in the night air for a few minutes. An alternative method is to turn on a hot shower and close the bathroom door so the bathroom fills with steam, then sit with the child in the steam.

The child needs immediate medical attention when symptoms

- last longer than three days
- include a fever higher than 102°F
- suggest that the child is not getting enough oxygen, such as CYANOSIS (blue lips)
- include excessive drooling

Though frightening for parents, croup is most often self-limiting and has few complications. Because croup is viral, ANTIBIOTIC MEDICATIONS do not bring about any improvement in symptoms. And, being viral, croup is contagious, spread through droplets in the air from coughing as well as by hand contact.

See also BREATH SOUNDS; EPIGLOTTITIS; PERTUSSIS.

D–E

deafness See HEARING LOSS.

dental caries The clinical term for cavities, erosions through the enamel of the TEETH that expose the inner pulp and sometimes the NERVE of the tooth. A dentist is the health-care provider who diagnoses and treats dental caries. Untreated dental caries can lead to INFECTION of the tooth's root structure and potentially an ABSCESS of the nerve canal, health conditions that require treatment with ANTIBIOTIC MEDICATIONS as well as dental care. The accumulation of BACTERIA can contribute to HALITOSIS (bad breath). A cavity that penetrates into the inner tooth often causes TOOTHACHE. Appropriate ORAL HYGIENE and routine dental care can help prevent dental caries.

See also GINGIVITIS; PERIODONTAL DISEASE.

ear The structures of the ear support the functions of hearing and balance. The ear has three divisions:

- The outer ear consists of the auricle (pinna) and auditory canal, structures that collect, focus, and channel sound waves.
- The middle ear consists of the auditory ossicles, three tiny bones that vibrate in sequence to focus and amplify sound.
- The inner ear contains the COCHLEA, which converts sound waves to NERVE impulses, and the structures of the vestibular system that regulate balance, the bony labyrinth, and the semicircular canals.

The TYMPANIC MEMBRANE, or eardrum, separates the outer ear and the middle ear; the EUSTACHIAN TUBE connects the middle ear with the THROAT to equalize pressure on both sides of the eardrum. Many causes of HEARING LOSS arise as a result of damage to or dysfunction of the structures of the outer and middle ear. The inner ear is entirely sealed from the external environment. Fluid bathes the delicate structures of the inner ear, helping protect them as well as isolate them from external stimuli that could affect their functions. Most disturbances of balance, often called vestibular dysfunction, stem from problems with the inner ear.

COMMON CONDITIONS AFFECTING THE EAR, HEARING, AND BALANCE

ACOUSTIC NEUROMA	BAROTRAUMA
CHOLESTEATOMA	HEARING LOSS
LABYRINTHITIS	MÉNIÈRE'S DISEASE
MYRINGITIS	OTITIS (INFECTION)
OTOSCLEROSIS	OTOTOXICITY
TINNITIS	VERTIGO

For further discussion of the ear within the context of otolaryngologic structure and function, please see the overview section "The Ear, Nose, Mouth, and Throat."

See also AUDIOLOGIC ASSESSMENT; COCHLEAR IMPLANT; HEARING AID.

earache A generalized term for sensations of pressure, discomfort, and PAIN in the area of the EAR. Pain messages from other structures of the head and neck, such as the NOSE and THROAT, also sometimes appear to come from the ear (referred pain). A common cause of earache in children is OTITIS media (INFECTION of the middle ear).

Congestion in the eustachian tubes can cause fluid to accumulate between the TYMPANIC MEMBRANE (eardrum) and the inner ear, creating increased pressure, which causes pain. A child

who is too young to speak may pull or tug at the ears. INFLAMMATION or infection of the auditory canal, commonly called swimmer's ear, is a frequent cause of earache in older children and adults. Referred pain in adults may indicate health conditions such as temporomandibular JOINT (TMJ) disorder, dental problems, SINUSITIS, TONSILLITIS, and PHARYNGITIS.

Treatment depends on the underlying cause of the earache. ANTIHISTAMINE MEDICATIONS can reduce congestion due to allergic response. ANTIBIOTIC MEDICATIONS are necessary when the infection is bacterial. ANALGESIC MEDICATIONS to relieve pain, such as acetaminophen and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), can ease the discomfort while HEALING takes place. Generally, treating the underlying reason for the pain causes the earache to go away.

See also BAROTRAUMA; EUSTACHIAN TUBE; TEMPOROMANDIBULAR DISORDERS.

eardrum See TYMPANIC MEMBRANE.

ear lavage Gentle flushing of the outer EAR to remove accumulated CERUMEN or foreign objects. Typically a health-care provider performs ear lavage in the doctor's office or a clinical setting, using a bulb syringe to instill warm water or other liquid and a basin to collect the solution as it drains from the auditory canal (ear canal). Ear lavage generally does not cause discomfort. People who have middle or inner ear disorders, vestibular disorders, or MYRINGOTOMY tubes in place should not undergo ear lavage.

See also CLEANING THE EAR; FOREIGN OBJECTS IN THE EAR OR NOSE.

ear wax See CERUMEN.

electrolarynx A handheld device that makes speech possible for people who have undergone LARYNGECTOMY (surgical removal of the larynx) or whose larynx is otherwise nonfunctional. The normal larynx consists of the VOCAL CORDS, CARTILAGE, MUSCLE, and ligaments. These tissues vibrate to generate the sounds the structures of the MOUTH convert into speech. The electrolarynx uses a rapidly moving diaphragm to generate vibrations that can help restore speaking ability.

There are two kinds of electrolarynx in common use:

- The transcervical electrolarynx rests against the neck or the cheek and sends vibrations through the muscles of the neck. Similar in appearance to a small flashlight, the transcervical electrolarynx requires one hand to hold it in place and has a finger-activated switch.
- The intraoral electrolarynx uses a small tube, somewhat like a straw, that rests along the inside of the cheek and sends vibrations directly to the structures of the mouth. Some models mount components in a denture or orthodontic device. An external amplifier and speaker project the sound.

Nearly all models of either kind operate on batteries and are easy for most people to use. The transcervical electrolarynx requires enough remaining healthy muscle tissue in the neck to transmit vibration. It is not a viable option when there is extensive tissue loss due to injury, such as trauma or BURNS, or surgery, such as for laryngeal CANCER. The vibrating diaphragm of the electrolarynx cannot produce the same intensity or range of tone as the natural structures of the healthy larynx, resulting in speech that tends to be machine-like and difficult to understand.

See also ESOPHAGEAL SPEECH; LIGAMENT; SMOKING AND CANCER; TRACHEOSTOMY.

epiglottitis A severe and rapidly progressing INFECTION of the epiglottis, a broad flap of tissue in the back of the THROAT that closes when swallowing to prevent food from entering the TRACHEA (windpipe). Epiglottitis brings on severe swelling in the throat, obstructing the flow of air through the trachea. Death can occur in minutes if the swelling completely blocks the airway.

Epiglottitis is a medical emergency that requires immediate hospital care.

Although epiglottitis can affect people of any age, it most commonly occurs in children ages two to seven years. The main cause of epiglottitis in children is bacterial infection with *Haemophilus influenzae* type b (Hib). In adults, epiglottis gener-

ally follows bacterial PHARYNGITIS such as "strep" throat.

Symptoms of the infection begin suddenly and worsen rapidly. Key symptoms include

- sore throat
- high FEVER (above 102°F)
- gasping for breath and stridor (high-pitched sounds on inhalation)
- profuse drooling
- desire to sit upright with the neck extended and the head tilted forward

Treatment is immediate hospitalization for administration of intravenous ANTIBIOTIC MEDICATIONS and often insertion of a breathing tube to maintain breathing until the swelling subsides. This course of treatment typically brings the infection under control within 48 to 72 hours, though hospitalization may be necessary for a week or longer. Prompt medical treatment of epiglottitis usually leads to complete recovery. The routine IMMUNIZATION of infants and children with the Hib vaccine has greatly contributed to the steady decrease in instances of this life-threatening infection.

See also BACTERIA; BREATH SOUNDS; TONSILLITIS.

epistaxis The clinical term for a bloody NOSE. The inner nasal passages have a rich and plentiful supply of BLOOD vessels, and there are many causes for epistaxis. During an episode of epistaxis, blood may come from the nostrils or from the back of the nose and into the nasopharynx (back of the THROAT). Most people who have normal clotting do not lose a significant amount of blood during an epistaxis episode, even when bleeding appears profuse. Blood loss often appears greater than it is because the blood mixes with nasal secretions.

To slow or stop epistaxis:

1. Keep the head upright.
2. Apply firm pressure to both nostrils using the thumb and forefinger.
3. Hold the pressure for at least 10 minutes without release.

The most common causes of epistaxis are injuries due to local irritation (notably insertion of fingers, especially in children, and presence of foreign objects in the nasal passages), BREATHING dry and especially cold air, heavy sneezing, nasal polyps, and external trauma such as a blow to the nose or face. Epistaxis may also indicate deviated septum, which alters the flow of air through the nostrils and exposes the nasal lining to chronic irritation.

People who have bleeding disorders, regularly take NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) including aspirin, or who have uncontrolled HYPERTENSION (high BLOOD PRESSURE) are more likely to experience heavy epistaxis, though these circumstances do not usually cause the bleeding. Epistaxis is usually self-limiting (the bleeding stops following initial treatment) and does not require a doctor's attention.

A doctor should evaluate bleeding that persists after taking basic measures to stop the nosebleed. A heavy blood flow may require, with local anesthetic, cauterization to seal the bleeding area or medicated packing (gauze strips, absorbent pledgets, or nasal tampons) placed into the area of the bleeding to hold continuous pressure against the blood vessels. Doctors typically prescribe a course of oral ANTIBIOTIC MEDICATIONS when it is necessary to place nasal packing, to safeguard against SINUSITIS (bacterial INFECTION of the SINUSES) or TOXIC SHOCK SYNDROME (a serious systemic bacterial infection). The doctor must remove any nasal packing, typically three days after its placement.

When extended treatment becomes necessary, the doctor will also request blood tests to assess blood cell counts and CLOTTING FACTORS and may choose to admit the person to the hospital for monitoring of the bleeding as well as the ability to maintain adequate breathing. Severe bleeding may require BLOOD TRANSFUSION or infusions of clotting factors. Rarely surgery is necessary to halt the bleeding, usually when the cause is external trauma or there are underlying health conditions that prevent the body's clotting mechanisms from properly functioning. Most often epistaxis is a minor problem that quickly resolves, though a doctor should evaluate recurring nosebleeds.

See also BACTERIA; BLEEDING CONTROL; COAGULATION; NASAL POLYP; SEPTAL DEVIATION; THROMBOCYTOPENIA.

esophageal speech A learned method to restore verbal communication for people who have undergone LARYNGECTOMY (surgical removal of the larynx, or voice box). When the THROAT is intact, air coming out of the LUNGS passes through the VOCAL CORDS and other structures of the larynx, generating sound vibrations that travel to the MOUTH. The mouth then forms these vibrations into words. Laryngectomy removes the throat; air instead enters and leaves the TRACHEA through a surgically created opening, or stoma. For esophageal speech, the person takes air into the mouth and swallows it, which sends the air into the ESOPHAGUS (tube that carries food to the STOMACH). When the esophagus expels the air back into the mouth, the force of the moving air generates sound in the form of a burp or belch. The mouth then forms these bursts of air into words. The technique takes considerable practice; however, it is possible produce a fairly natural voice, although certain sounds may be difficult to form and understand.

Tracheoesophageal speech is a variation of esophageal speech in which the surgeon creates an opening between the trachea and the esophagus at the point of the stoma, called a tracheoesophageal puncture, and inserts a small shunt (connecting tube) with a one-way valve. The person then learns to force air from the trachea into the esophagus instead of taking air in through the mouth and forcing it into the esophagus. This is somewhat more natural and many people find it an easier technique to master.

See also ELECTROLARYNX.

eustachian tube An elongated, valvelike channel of tissue that connects the middle EAR and the THROAT. The eustachian tube relaxes or constricts to equalize the pressure between the middle ear and the external environment. The sensation of the ears "popping" indicates air moving through the eustachian tube. Congestion easily blocks the eustachian tube, particularly in children because their small, compact facial structure causes the eustachian tubes to be nearly horizontal. In adults, the eustachian tubes angle downward from the ear to the throat, thwarting progression of fluid from the throat to the middle ear. Blocked eustachian tubes result in a feeling of fullness in the ears and can set the stage for OTITIS media (INFECTION of the middle ear).

For further discussion of the eustachian tubes within the context of otolaryngologic structure and function, please see the overview section "The Ear, Nose, Mouth, and Throat."

See also PHARYNGITIS.

F

foreign objects in the ear or nose Material that enters the EAR or NOSE. This is a common occurrence with young children, who tend to put objects into their noses and ears. Typically, the object is visible, though drainage or odor may signal an undetected obstruction that is causing an INFECTION. Attempts to retrieve or clear the object can result in pushing it instead farther into the auditory canal or nasal passages; there is a risk with foreign objects in the nose of inhaling them into the airways or LUNGS. A health-care provider should assess and remove any foreign object that does not come out of the ear or nose with minimal effort, as well as any circumstance in which an infection might exist. Particles of food and objects such as paper wads attract moisture and can swell, lodging more firmly in the ear or nose.

To treat an insect in the ear:

1. Lie on the side with the affected ear up.
2. Use an eyedropper to gently fill the auditory canal with warm mineral oil or olive oil.
3. Wait a few minutes for the oil to suffocate the insect.
4. Often the insect will float to the top of the canal. If it does not, turn the head so the affected ear is down and allow the oil to drain from the auditory canal, bringing the insect with it.

Do NOT put water into the ear canal in an attempt to remove an insect or other foreign object. Water may cause the insect or object to swell, lodging it more firmly into the ear canal.

When there is an object in the nose:

1. Breathe through the mouth to avoid inhaling the object or lodging it farther into the nasal passages.
2. Hold the clear nostril shut and breathe out through the blocked nostril.
3. Do not blow forcefully or insert anything into the nose to attempt to prod or pull the object free.

If these techniques are not effective, a health-care provider will need to remove the object. Removal of the foreign object is nearly always a complete remedy, unless there is a secondary infection that requires further treatment.

See also BLOWING THE NOSE; CLEANING THE EAR; EAR LAVAGE.

G

gag reflex A rapid and intense contraction of the pharyngeal muscles to expel material before it enters the THROAT. Touching the back of the soft palate activates the gag REFLEX in most people, causing a retching action. The gag reflex is more sensitive in some people, interfering with health examinations of the throat or dental examinations and treatment. HYPNOSIS and BIOFEEDBACK are two methods by which people can learn to delay or minimize the gag reflex. Health conditions that can activate the gag reflex include severe PHARYNGITIS, EPIGLOTTITIS, and profuse POSTNASAL DRIP. Sprays to anesthetize the throat, such as to treat relieve sore throat PAIN or for ENDOSCOPY procedures, temporarily numb the nerves in the soft palate to subdue the gag reflex. A reduced or absent gag reflex, which can result in potentially life-threatening ASPIRATION, may occur with STROKE and neurologic disorders such as CEREBRAL PALSY and PARKINSON'S DISEASE.

See also SWALLOWING DISORDERS.

gingivitis INFLAMMATION of the gum tissue around the TEETH. Most gingivitis is an early form of PERIODONTAL DISEASE. Signs of gingivitis include painless bleeding (spontaneous or with brushing) and swollen gums that may be bright red or shiny. Some people develop painless sores or ulcerations on the gums that indicate INFECTION. Though people may seek medical care because of the bleeding, dentists and periodontists provide dental-based care for gingivitis. People who have DIABETES, people who smoke cigarettes, or use smokeless tobacco, and women who are pregnant have increased susceptibility for gingivitis.

See also CANKER SORE; DENTAL CARIES; ORAL HYGIENE; SMOKING AND HEALTH.

glossitis An INFLAMMATION of the tongue that is typically the result of irritation, viral or bacterial INFECTION, vitamin B deficiency, or ANEMIA. Glossitis may also develop as an opportunistic condition in people who have IMMUNE SYSTEM disorders.

A rare though potentially life-threatening complication of glossitis is swelling that causes the tongue to block the airway. This requires emergency medical attention.

In glossitis, the tongue often hurts, has a characteristic "beefy" appearance, and has a surface that is deep red and smooth. Swallowing and speaking may be difficult. Most glossitis responds to corticosteroid mouthrinses to reduce the inflammation. Mouthrinses with diphenhydramine may also bring relief. A bacterial infection requires treatment with ANTIBIOTIC MEDICATIONS; a yeast infection requires treatment with ANTIFUNGAL MEDICATIONS. Dietary changes or nutritional supplements are necessary when vitamin B or iron deficiency is the cause. Appropriate treatment typically resolves the symptoms, and the tongue returns to normal.

See also BACTERIA; HALITOSIS; ORAL HYGIENE.

H

hairy tongue The common term for the circumstance of overgrown filiform papillae on the tongue, a condition known clinically as lingua villosa. Filiform papillae are long, resemble hairs, and do not contain taste buds. Their purpose is to help move food during chewing and swallowing. Normally the wear and tear of this function breaks them off, a process called desquamation. Various circumstances inhibit desquamation, allowing the filiform papillae to grow up to 10 times longer than normal. The overgrown filiform papillae then trap food debris and other substances that impart color (such as coffee and tea), giving the characteristic "colored hair" appearance of hairy tongue. The causes of hairy tongue are numerous and include eating habits centered around soft foods, which do not scrape the tongue, and inadequate ORAL HYGIENE.

From a medical perspective hairy tongue is harmless, though people in whom it develops tend to find it aesthetically displeasing and in some it tickles or irritates the soft palate during swallowing. Brushing the tongue as a routine aspect of oral hygiene, or using a tongue scraper, nearly always restores the desquamation process and reduces the length of the filiform papillae. Hairy tongue is also slang for a bad hangover, probably stemming from the correlation between chronic ALCOHOL abuse and poor oral hygiene habits.

See also HALITOSIS.

halitosis The clinical term for bad breath. Halitosis can indicate numerous local or systemic health conditions. Local halitosis occurs when an abundance of BACTERIA that release sulfur as a waste byproduct colonize in the mouth. Systemic halitosis occurs as a response to metabolic and chemical changes that the disease process causes in the body.

LOCAL CAUSES OF HALITOSIS	SYSTEMIC CAUSES OF HALITOSIS
poor ORAL HYGIENE	PEPTIC ULCER DISEASE
food stuck between TEETH	GASTROESOPHAGEAL REFLUX DISORDER (GERD)
inadequate saliva production	certain cancers
TONSILLITIS, adenoiditis, SINUSITIS	DIABETES
POSTNASAL DRIP	LIVER disease
	kidney disease

Treatment for underlying conditions often reduces or eliminates halitosis. When the source is ineffective ORAL HYGIENE, improved brushing and flossing techniques can help clean food debris from the MOUTH, which reduces the presence of sulfur-producing bacteria. Medications can cause dry mouth and even leave unpleasant odors in the mouth. Some people are predisposed to mouth conditions that support the presence of bacteria. Typically, a dentist treats halitosis related to oral hygiene, PERIODONTAL DISEASE, DENTAL CARIES, and other dental conditions. A doctor may recommend approaches to minimize halitosis that exists secondary to other health conditions. Thyme, eucalyptus, peppermint, and caraway are among the herbal remedies for halitosis.

See also GINGIVITIS; GLOSSITIS; HAIRY TONGUE.

hearing aid An external device that amplifies sound to compensate for HEARING LOSS. A hearing aid incorporates a receiver (microphone) to pick up sound waves, an amplifier to magnify the sound waves, and a battery that powers the receiver and amplifier. Sound quality with a hearing aid is different from sound quality the natural EAR perceives, and it takes time to become accustomed to using hearing aids. Hearing aids cannot restore normal hearing though they can increase

the range of frequency and pitch the ear can detect through amplification and modulation. Hearing aids are most effective in sensorineural hearing loss and can improve hearing in one ear or both ears.

Kinds of Hearing Aids

There are five kinds of hearing aids in common use today:

- Completely in the canal (CIC) hearing aids are the smallest available and fit well into the auditory canal. They are barely visible when in place. CIC hearing aids are most effective for mild to moderate hearing loss. People who have small auditory canals or limited manual dexterity may not be able to use CIC hearing aids. CIC hearing aids allow the wearer to use the telephone without adaptive devices.
- In the canal (ITC) hearing aids fit into the start of the auditory canal. A bit larger than CIC hearing aids, ITC hearing aids are somewhat noticeable when in place. They are easier to handle than CIC hearing aids and also are most effective for mild to moderate hearing loss.
- In the ear (ITE) hearing aids fit at the opening of the auditory canal and are visible on the outer ear (auricle). The larger size of ITE hearing aids give them the capacity to contain larger amplifiers, extending the range of hearing loss they can accommodate. ITE hearing aids are effective for mild to moderately severe hearing loss.
- Behind the ear (BTE) hearing aids drape over the external ear (auricle), with the housing for the electronics and battery behind the ear. A thin tube runs from the BTE hearing aid over the front of the auricle and into the auditory canal. BTE hearing aids accommodate the broadest range of hearing loss because they can hold larger amplifiers and the larger batteries necessary to provide power.
- Implantable middle ear devices are surgically implanted in the middle ear. They attach to and directly stimulate the auditory ossicles, the tiny bones in the middle ear that amplify and transmit sound to the inner ear. There are two variations of implantable middle ear devices, one that is completely implanted (with the receiver embedded in a pouch of tissue behind the ear) and one that has internal and external components (the receiver hangs behind the ear). Implantable middle ear devices accommodate moderate to severe hearing loss and typically become an option when conventional external hearing aids are ineffective.

One other style, the body hearing aid, attaches to the belt or fits within a pocket. About the size of a cellular phone, the body hearing aid can contain a very large amplifier and comparable battery to power it. Wires run from the body hearing aid unit to the ears. Though significantly less convenient than other styles of hearing aids, the body hearing aid can make limited HEALING possible for people with profound hearing loss.

BTE hearing aids can be analog or digital; CIC, ITC, and ITE hearing aids and implantable middle ear devices are digital. Analog units receive incoming sound waves and transmit them directly to the amplifier; they make sound only louder. Many people consider analog technology outdated, though it nonetheless provides improved hearing across a broad spectrum of hearing loss. Some analog hearing aids have manual volume controls and others can accept a wider range of adjustment via computer programming. Digital hearing aids convert incoming sound waves to binary signals that are much faster to process electronically. Many digital models use computer microchips to allow a broad range of customized adjustments that can filter out certain sounds (such as background noise) and independently enhance or subdue specific frequencies of sound. Digital hearing aids are programmable and provide sounds closer to natural hearing, though they are significantly more expensive than analog hearing aids. For many people cost is a framing factor in choosing a hearing aid because most health insurance plans do not provide coverage for hearing aids.

Adjusting to Hearing Aids

Hearing aids cannot replace natural hearing or restore the function of hearing to normal. Simplistically, hearing aids overstimulate the remaining sensorineural structures of the inner ear so they can respond to sound signals. People using hear-

ing aids must learn to consciously filter unnecessary noise and sounds. In natural hearing, the structures of the ear and the BRAIN work in close integration to receive, transmit, and interpret sound waves. Hearing aids disrupt that integration. Sound interpretation becomes a conscious activity, though with practice it becomes automatic. It takes concentration and focus to participate in ordinary conversation, and many people find the effort tiring even when they become proficient at it. However, most people find the effort a reasonable trade-off for the return of some hearing ability.

See also COCHLEAR IMPLANT; QUALITY OF LIFE; SIGN LANGUAGE.

hearing loss The diminishment of hearing ability. Hearing loss can be temporary or permanent, sudden or progressive, unilateral (affect only one EAR) or bilateral (affect both ears), partial or profound (total), congenital or acquired. There are two kinds of hearing loss: sensorineural (NERVE) and conductive. About 28 million Americans have some level of hearing loss; 30 percent of them are over age 65 and 20 percent are under age 18. About 1 in 1,000 infants born in the United States each year has a congenital hearing loss.

Though there are numerous dimensions to hearing, audiologists measure hearing loss in terms of sound intensity. Healthy human hearing perceives tones between frequencies of 500 Hz (very low) and 4,000 Hz (very high). AUDIOLOGIC ASSESSMENT measures the intensity of sound required to hear tones at certain levels within the range of normal hearing and reports deviations in decibels (dB) of loss. Hearing loss begins when the level of loss reaches 16 dB. Health experts classify hearing loss greater than 90 dB as profound; at this level the ability to hear the normal sounds of everyday activities is lost. Though profound hearing loss can occur in only one ear, the term typically refers to lack of hearing in both ears. Most health-care providers use the American Speech-Language-Hearing Association (ASLHA) classification system for assessing the degree of hearing loss.

Hearing loss may result from damage (congenital or acquired) to the nerves and related structures of the inner ear that receive and transmit sound signals to the BRAIN; this is sensorineural hearing loss. It accounts for 90 percent of all hearing loss and is usually permanent. Hearing loss also may result from circumstances that prevent sound waves from traveling through the outer and middle ears; this is conductive hearing loss and is often correctable with medications or surgery. Temporary conductive hearing loss is common, especially in children who have middle ear infections (OTITIS media). Congestion due to COLDS and allergies is a common cause of temporary con-

DEGREE OF HEARING LOSS

Classification	Level of Loss	Loss Threshold
minimal (slight)	16 to 25 dB	ticking of a watch, normal BREATHING
mild	26 to 30 dB	hum of electrical appliances
moderate	31 to 50 dB	falling rain, whispering, residential neighborhood noise, library, typical office, normal voice of a child
moderately severe	51 to 70 dB	normal conversation, washing machine, sewing machine, vacuum cleaner, birds, freeway traffic, normal television volume
severe	71 to 90 dB	telephone ringing, alarm clock, doorbell, city traffic, noisy restaurant, flushing toilet
profound	91 db or greater	hair dryer, small power tools, crying infant, shouting, police/fire/medical aid siren

ductive hearing loss in adults. Compacted CERUMEN (ear wax) in the auditory canal and OTOSCLEROSIS (fusion of the auditory ossicles, the tiny bones of the middle ear) are common causes of treatable conductive hearing loss. Damage to the areas of the brain that process hearing, speech, and language can result in auditory processing disorders in which, though the structures and mechanical functions of hearing may remain intact, the person cannot understand spoken words. Typically other language impairments, such as the abilities to read and write, also exist with auditory processing disorders.

Hearing loss in children, whether congenital or acquired, has significant developmental consequences. It is now the standard of care in the United States to test newborns for hearing in the first few weeks of life, with regular screening for hearing difficulties at well child checks and routine medical examinations through ADOLESCENCE. The ability to hear forms the basis for understanding language. Early intervention to correct or accommodate hearing loss in prelingual children is essential for appropriate development and communication. A teacher's voice in a classroom projects an intensity of about 70 dB; children with hearing loss at this level or greater will be unable to hear in school.

The majority of hearing loss in adults is acquired. Excessive noise exposure and changes related to aging (PRESBYCUSIS) are the most common causes of acquired adult hearing loss. Hearing loss may also result from health conditions, such as ACOUSTIC NEUROMA and MÉNIÈRE'S DISEASE, that interfere with the functions of hearing. Trauma, such as FRACTURE of the bones in the face and head or BURNS that damage the external ear, can cause hearing loss. Various medications, including certain antibiotics, diuretics, antihypertensives, high doses of aspirin, and CHEMOTHERAPY drugs, also can damage or destroy hearing.

Symptoms and Diagnostic Path

Sudden hearing loss in adults is typically obvious. Progressive hearing loss is often subtle and noticed more by others than the person experiencing the loss. Common indicators of diminishing hearing ability include

- perception that "everyone" mumbles when speaking
- unable to hear the telephone or doorbell ring
- volume is past the halfway mark when listening to television or radio
- easier to hear someone talking when looking directly at him or her
- restaurants are "too noisy" for conversation

TINNITUS (sensation of roaring or buzzing sound in one ear or both ears) may be an early sign of sensorineural hearing loss. Children with undetected hearing loss may fail to respond when spoken to or to follow instructions, have difficulty in school, seem to mumble or slur their words, or be developmentally delayed especially in language skills.

Diagnosing hearing loss begins with physical examination of the outer and middle ears to look for obvious problems such as compacted cerumen, inflamed or damaged TYMPANIC MEMBRANE (eardrum), and structural anomalies. An audiologic assessment then measures hearing response to a variety of tests. If questions remain about the cause of the hearing loss, the doctor may request COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI).

Treatment Options and Outlook

Medical or surgical treatments can restore most conductive hearing loss. Sensorineural hearing loss requires interventions such as hearing aids, which amplify sound, or cochlear implants, which directly stimulate nerve cells in the inner ear. Hearing lost as a result of health conditions such as acoustic neuroma often returns when the neuroma is removed. Accommodations for profound hearing loss include training in lip reading and SIGN LANGUAGE.

Hearing loss, however subtle, can significantly affect on a person's ability to function in, and enjoy, everyday life. Even mild to moderate hearing loss removes many common sounds from daily experience. Early intervention and appropriate accommodation can mitigate to the extent possible much hearing loss. Hearing aids, though they cannot restore normal sound quality and hearing, make it possible to participate in conversation and to hear

many of the sounds that provide orientation to one's personal environment. With accommodation, most people with hearing loss are able to fully participate in nearly all activities those who have normal hearing can experience. In the United States, the Americans with Disabilities Act (ADA) requires public facilities and most employers to provide reasonable accommodations for people who have profound hearing loss.

Risk Factors and Preventive Measures

The most significant risk factors for acquired hearing loss are age and noise exposure. Researchers are exploring the processes of aging that cause hearing loss, looking for ways to mitigate or eliminate them. Limiting noise exposure appears to be one way to help reduce sensorineural hearing loss, even as a component of aging. Just 15 minutes of exposure to noise at greater than 115 dB (jet engine, chain saw, rock concert, sporting event in a stadium or arena) damages the HAIR cells within the cochlea. The US Occupational Safety and Health Administration (OSHA) establishes guidelines and regulations for protection from exposure to noise in the workplace. Other mechanisms that contribute to age-related hearing loss are likely genetic; research continues in this area as well.

Because numerous medications can damage the structures of the inner ear, it is important to always ask the doctor or pharmacist whether this is a potential SIDE EFFECT. When it is, ask if there are alternatives that are less risky for hearing. Illnesses such as MEASLES, though now less common because of vaccines, also can cause hearing loss. RUBELLA (German measles) remains a leading cause of congenital hearing loss.

See also APHASIA; BAROTRAUMA; NOISE EXPOSURE AND HEARING; OTOTOXICITY; PRENATAL CARE.

labyrinthitis An INFLAMMATION or INFECTION of the vestibular system, the body's balance mechanism within the inner EAR. The sudden onset of VERTIGO (feeling of spinning) is the characteristic symptom. Many people also experience transitory or temporary hearing problems and TINNITUS (a ringing or roaring sound). When an infection is present, it can be viral or bacterial. Bacterial labyrinthitis typically develops as a consequence of chronic OTITIS media (middle ear infection). Doctors believe viral labyrinthitis develops when the bloodstream carries a VIRUS into the inner ear. Inflammatory labyrinthitis may be an autoimmune condition; doctors are not certain of its etiology (origin and development). It is sometimes difficult to diagnose and distinguish the kind of labyrinthitis because access to the inner ear is so limited. Often in bacterial labyrinthitis there are signs of infection around the TYMPANIC MEMBRANE (eardrum), or might be signs of infection elsewhere including the mastoid (MASTOIDITIS) and less commonly, MENINGITIS.

Bacterial labyrinthitis has potentially serious complications, including destruction of the labyrinth and COCHLEA, which results in permanent and profound HEARING LOSS. It requires treatment with ANTIBIOTIC MEDICATIONS. Untreated bacterial labyrinthitis also can extend into other infections such as mastoiditis and meningitis. Viral labyrinthitis and inflammatory labyrinthitis generally do not leave lasting damage. Because distinguishing the cause of labyrinthitis is sometimes difficult and the consequences of untreated bacterial labyrinthitis can be severe, doctors typically prescribe antibiotics when the diagnosis is unclear, even though antibiotics will not treat viral labyrinthitis. Sometimes medications to suppress vertigo and resulting NAUSEA are also necessary, at least until the inflammation or infection is under control.

See also ACOUSTIC NEUROMA; BACTERIA; BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV); MÉNIÈRE'S DISEASE; VESTIBULAR NEURONITIS.

laryngectomy Surgical removal of the larynx, which includes the VOCAL CORDS and other structures that produce sound for the function of speech. Surgeons perform the majority of laryngectomies to treat CANCER due to cigarette smoking. Laryngectomy results in the loss of the ability to speak.

In laryngectomy, the surgeon makes an incision in the neck and removes the structures of the larynx, typically including the vocal cords and upper portion of the TRACHEA as well as surrounding MUSCLE tissue to obtain a cancer-free margin. The ESOPHAGUS, which carries food from the MOUTH to the STOMACH, remains intact. In the OPERATION's final stage the surgeon creates a permanent opening through the neck into the trachea, called a stoma, for BREATHING.

The operation takes five to eight hours for the surgeon to perform, and most people stay in the hospital for 10 to 14 days following the surgery. Rehabilitation begins immediately and includes instruction to care for the stoma as well as swallowing exercises. Many people also start to learn ESOPHAGEAL SPEECH, though speech therapy is most extensive during outpatient rehabilitation following discharge from the hospital. The surgical wound heals completely in about six to eight weeks.

Occasionally doctors diagnose the cancer early enough to permit a partial laryngectomy, in which the surgeon removes only the tumor and tissues

in proximity to it. With partial laryngectomy the airway and often part of the vocal structures remain intact, so breathing and speech are normal after recovery, though the quality and volume of the voice may change.

See also CANCER RISK FACTORS; CANCER TREATMENT OPTIONS AND DECISIONS; ELECTROLARYNX; HEALING; SMOKING AND CANCER; SMOKING AND HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT.

laryngitis Irritation or INFLAMMATION of the larynx (voice box) that results in hoarseness or loss of voice. Most laryngitis is viral, though may accompany or follow a bacterial INFECTION such as STREP THROAT. Laryngitis is also common in people who strain their voices through loud singing, yelling, and extended talking, and in people who smoke or who work or live in environments that are smoky. Resting the voice by speaking softly (though not whispering as it further stresses the tissues of the larynx) and sucking on hard candy or COUGH drops help soothe the irritated tissues. A cool-mist humidifier, especially when sleeping, helps reduce irritation. Most laryngitis goes away within 10 to 14 days and does not need medical treatment. Bacterial laryngitis requires treatment with an appropriate ANTIBIOTIC MEDICATIONS.

A doctor should evaluate laryngitis when:

- hoarseness/discomfort last longer than 14 days
- an accompanying cough produces yellow or green sputum
- FEVER is greater than 101°F

Frequent or extended laryngitis might indicate the presence of VOCAL CORD NODULE, VOCAL CORD POLYP, or laryngeal CANCER.

See also BOGART-BACALL SYNDROME; COLDS; EPIGLOTTITIS; PHARYNGITIS; SMOKING AND HEALTH; TONSILLITIS; VIRUS.

laryngocele An air-filled bulge (herniation) that develops within the tissues of the larynx (voice box), often among the folds of the VOCAL CORDS. Laryngocele may be present at birth as a CONGENITAL ANOMALY or develop later in life, often as a consequence of persistent pressure against the structures of the THROAT. A congenital laryngocele may not cause symptoms until environmental stressors that create increased laryngeal pressure cause it to enlarge. Musicians who play wind instruments are particularly vulnerable to laryngoceles, as are people with OBSTRUCTIVE SLEEP APNEA. Occasionally a laryngeal tumor causes a laryngocele.

Hoarseness, a feeling that there is something caught in the throat, dry COUGH, and a soft lump visible on the external throat are among the most common symptoms. A large laryngocele can cause stridor (a high-pitched noise with inhalation) and difficulty swallowing. The diagnostic path typically includes COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) of the throat and laryngoscopy (examining the inside of the throat through a lighted, flexible scope). Because a laryngocele presents a prime opportunity to trap BACTERIA that cause INFECTION as well as the potential to interfere with BREATHING and swallowing, the treatment of choice is an OPERATION through an incision in the neck to close or remove the laryngocele.

See also BREATH SOUNDS; ENDOSCOPY; SWALLOWING DISORDERS.

leukoplakia Precancerous patches, or lesions, inside the MOUTH. The patches are light-colored and most commonly form on the tongue and insides of the cheeks. Irritation to these tissues over time, such as from all forms of tobacco use and poorly fitting dentures or dental bridges, causes leukoplakia to develop. In a type of leukoplakia specific to people with HIV or AIDS, hairy leukoplakia, the patches look like white fuzz. Hairy leukoplakia often is one of the earliest signs of HIV INFECTION. Leukoplakia may also affect the VULVA in women. Biopsy to examine the cells of the patches confirms the diagnosis. In some people, removing the source of the irritation causes the leukoplakia to go away. Often doctors prefer to remove the lesions surgically, which generally is an office procedure with local ANESTHESIA. When the irritation continues, or in the presence of HIV/AIDS, leukoplakia may return.

See also ORAL HYGIENE; SMOKING AND CANCER; SMOKING AND HEALTH; TOBACCO USE OTHER THAN SMOKING.

M

mastoiditis An INFECTION in the mastoid BONE behind the EAR. Mastoiditis typically develops as a consequence of untreated or chronic OTITIS media (middle ear infection) when BACTERIA migrate from the middle ear to the adjacent mastoid bone. The rather porous structure of the mastoid bone, which is more a collection of small cavities than a solid structure, provides an ideal habitat for bacteria. Untreated mastoiditis can spread to the nasal SINUSES as well as the MENINGES (membranes surrounding the BRAIN and SPINAL CORD), causing bacterial MENINGITIS, and to the brain itself, causing ENCEPHALITIS. These infections are potentially fatal and require immediate medical treatment. Though mastoiditis was once a common cause of childhood death, it has become rare since the advent of ANTIBIOTIC MEDICATIONS.

PAIN behind the ear, FEVER, and a recent episode of otitis media are the leading indications of acute mastoiditis. The person may also have swelling and tenderness in the mastoid area, and the auricle (external ear) may appear to stick out from the side of the head. Chronic mastoiditis may be subclinical; that is, the infection causes few overt symptoms until it spreads beyond the mastoid or destroys mastoid bone tissue. Diagnosis includes blood tests and cultures of any fluid in the ear to look for signs of infection, and occasionally COMPUTED TOMOGRAPHY (CT) SCAN. In most cases of acute mastoiditis, antibiotic medications and occasionally MYRINGOTOMY (insertion of a small tube through the TYMPANIC MEMBRANE to allow fluid to drain from the middle ear) successfully eradicate the infection. Chronic mastoiditis sometimes requires surgery to open, drain, and occasionally remove portions of the mastoid structure. Severe mastoiditis may require mastoidectomy, in which the surgeon removes the entire mastoid bone. Most people recover fully following treatment, though should have an AUDIOLOGIC ASSESSMENT to determine whether there is residual HEARING LOSS.

See also ABSCESS; SURGERY BENEFIT AND RISK ASSESSMENT.

Ménière's disease A disorder of the inner EAR that results in balance and hearing disturbances. Doctors do not know for certain what causes Ménière's disease. There are numerous approaches to treating the condition's symptoms though there is no known cure for the disease. The most significant consequence of Ménière's disease is permanent and progressive HEARING LOSS. About 2.5 million Americans have Ménière's disease.

The disease is also called endolymphatic hydrops, a reference to the dilation of the structure in the inner ear called the membranous labyrinth. Researchers believe the dilation signals an abnormal accumulation of fluid within the membranous labyrinth, though do not know what causes that accumulation. Current research suggests that the dilation results in small tears that allow the fluid within the membranous labyrinth, the endolymph, to mix with fluid outside the membranous labyrinth, the perilymph. The two fluids have different chemical compositions; some researchers believe changes in the electrolyte content that occur when the fluids mix cause vestibular dysfunction that results in the specific constellation of symptoms that define Ménière's disease. Continued or repeated dilation likely results in repeated tears and recurrent symptoms.

Symptoms and Diagnostic Path

Most otolaryngologists look for four cardinal, or defining, symptoms that occur with repeated

episodes (recurrent symptoms) when distinguishing Ménière's disease from other forms of vestibular dysfunction. These are

- VERTIGO (sensation that the person or the environment is spinning or whirling), often with NAUSEA and vomiting, and sometimes debilitating loss of balance
- TINNITUS (rushing or roaring sound) in one ear, often worse during vertigo attacks
- hearing loss in one ear that returns with the conclusion of each episode of symptoms though progressively worsens with multiple episodes
- sensation of fullness or congestion in one ear

Symptoms may last 20 minutes to several hours, and may fluctuate within, as well as vary among, episodes. Doctors disagree on whether all four symptoms must exist to constitute Ménière's disease, and whether symptoms other than vertigo must involve only one ear. Diagnosis is primarily by exclusion, with findings to rule out other vestibular dysfunctions and causes. Diagnostic tests and procedures often include

- OTOSCOPY (visualization of the auditory canal and middle ear with a lighted instrument)
- complete blood count (CBC) to look for signs of infection or immune response
- COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to rule out tumors and structural problems
- NEUROLOGIC EXAMINATION to rule out ACOUSTIC NEUROMA or disorders affecting the CRANIAL NERVES
- AUDIOLOGIC ASSESSMENT to evaluate hearing loss

Findings that fail to support any other diagnosis, in combination with the four cardinal symptoms, point to a diagnosis of Ménière's disease.

Treatment Options and Outlook

Treatment largely focuses on relieving symptoms and varies depending on the relief various efforts provide. Common treatments may include antinausea medications, anticholinergic medications, ANTIHISTAMINE MEDICATIONS, and scopolamine to reduce the vertigo. When the vertigo is such that it prohibits the activities of living for an extended time, surgically cutting the vestibular NERVE ends the nerve messages the labyrinth sends to the BRAIN yet preserves hearing. When vertigo is severe and hearing loss is complete, labyrinthectomy becomes a treatment option. The otolaryngologist may surgically remove the labyrinth or instill a DRUG, such as the antibiotic gentamicin, into the inner ear that chemically destroys the NERVE endings in the labyrinth.

The outlook for people who have Ménière's disease is variable and unpredictable. About 20 percent have only one attack; typically there are few long-term consequences when this is the case, though some people experience mild permanent hearing loss. About 40 percent have recurrent attacks, sometimes years apart, that medical treatments effectively mitigate. Hearing loss tends to worsen with each episode of symptoms, however, and can become profound (complete) in the affected ear. Another 20 percent have frequent and debilitating attacks that do not respond to medical treatments. For these people, Ménière's disease significantly interferes with QUALITY OF LIFE and often produces moderate to severe hearing loss over a relatively short period of time. The remaining 20 percent of people who have Ménière's disease fall along the continuum.

The most favorable improvement for those who have repeated episodes of symptoms is with vertigo, which seems to go away roughly 10 years after diagnosis in about 70 percent of people. Doctors have no explanation for this; though medical treatments can lessen the severity of vertigo during attacks, they do not appear to influence this 10-year resolution marker.

Risk Factors and Preventive Measures

There are no known measures to prevent Ménière's disease from developing in the first place. Lifestyle factors appear to influence the return and severity of symptoms in many people who have the condition, though researchers have yet to establish definitive connections. These factors include the amount of sodium in the diet, fluid consumption and balance, smoking, stress, and certain food triggers. Many people find that restricting dietary sodium and limiting fluid intake reduce the fre-

quency of episodes because it helps prevent the accumulation of fluid throughout the body, including in the inner ear. The doctor may also prescribe a diuretic medication to further minimize fluid retention. Local and online support groups can provide encouragement and anecdotal information about successful symptom management methods.

See also BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV); LABYRINTHITIS; PERIPHERAL NERVOUS SYSTEM; VESTIBULAR NEURONITIS.

mouth The facial structure that provides the sensory function of taste, performs the mechanics of speech, and prepares food for entry into the gastrointestinal system. The base of the skull establishes the roof of the mouth; the mandible, or lower jaw, establishes the floor of the mouth. The muscular cheeks help move food through the mouth during mastication (chewing) as well as shape the mouth for forming the sounds of speech. The tongue contains most of the taste buds, specialized papillae (or bumps) that contain the taste cells, though some taste buds appear on the soft palate and back of the THROAT. The tongue also moves food through the mouth and then pushes it to the top of the throat for swallowing. The tongue's shape and placement within the mouth help direct the flow of air and sound during speech. The TEETH function primarily to tear and pulverize food and also provide a solid structure for the tongue to push against during speech. SALIVARY GLANDS produce saliva, which keeps the inside of the mouth wet and aids in breaking down food to pass down the throat.

COMMON CONDITIONS AFFECTING THE STRUCTURES OF THE MOUTH

CANKER SORE	CLEFT PALATE/CLEFT PALATE AND LIP
COLD SORE	DENTAL CARIES
GLOSSITIS	HAIRY TONGUE
HALITOSIS	LEUKOPLAKIA
PERIODONTAL DISEASE	SIALADENITIS
SIALOLITHIASIS	SIALORRHEA
SPEECH DISORDER	THRUSH
TOOTHACHE	

For further discussion of the mouth within the context of otolaryngologic structure and function please see the overview section "The Ear, Nose, Mouth, and Throat."

See also NOSE.

myringitis INFLAMMATION and irritation of the TYMPANIC MEMBRANE (eardrum), usually as the result of a viral or bacterial INFECTION. The characteristic symptom is the sudden onset of PAIN, sometimes severe. Many people also experience temporary HEARING LOSS in the affected EAR. In bullous myringitis (also called myringitis bullosa), fluid-filled, blisterlike vesicles form on the tympanic membrane and cause intense pain. Sometimes the doctor lances, or carefully punctures with a MYRINGOTOMY scalpel, the vesicles to release the fluid and relieve the pain. OTITIS media, infection of the middle ear, can extend to involve the tympanic membrane. The pain associated with this form of myringitis often includes the sensation of pressure. Doctors typically prescribe ANTIBIOTIC MEDICATIONS to treat the infection and ANALGESIC MEDICATIONS to relieve the pain. Appropriate treatment resolves most myringitis in 10 to 14 days, and any temporary hearing loss returns. Occasionally myringitis causes the tympanic membrane to perforate, which may require further medical treatment.

See also RUPTURED EARDRUM; TYMPANOPLASTY.

myringotomy A surgical incision in the TYMPANIC MEMBRANE (eardrum) to allow fluid in the middle EAR to drain out. Fluid in the middle ear is a key symptom of OTITIS media (middle ear infection). The buildup of pressure causes considerable PAIN and can cause the tympanic membrane to perforate (tear or rupture). When otitis media is chronic or recurrent, the surgeon places a tympanostomy tube in the incision to retain a pathway for drainage to continue. The tube is very small and generally falls out within several months, then the opening in the tympanic membrane heals closed. The OPERATION is a same-day surgery done under general anesthetic, and usually takes no longer than 20 minutes per ear. Recovery is rapid.

See also MASTOIDITIS; RUPTURED EARDRUM; SURGERY BENEFIT AND RISK ASSESSMENT; TYMPANOPLASTY.

N

nasal polyp A noncancerous, fleshy growth within the interior NOSE. Polyps are outgrowths of the mucous membrane and extend from the membrane on a stemlike projection called a pedicle. Polyps have a rich BLOOD supply and bleed easily. Because of this and because there is a chance for them to become cancerous over time, doctors prefer to surgically remove them. Nasal polyps that form in the air passages and SINUSES can obstruct the flow of air, interfering with BREATHING. Chronic irritation (such as from ALLERGIC RHINITIS) and INFECTION (such as SINUSITIS) seem to encourage the growth of polyps; treating the underlying conditions helps prevent polyps from recurring. Multiple nasal polyps are common in people who have CYSTIC FIBROSIS.

See also INTESTINAL POLYP; VOCAL CORD POLYP.

nasal vestibulitis A bacterial INFECTION of the HAIR follicles around the base of the nostrils that results in INFLAMMATION and irritation of the tissues. Symptoms include redness, swelling, and PAIN. Sometimes the tissue becomes raw and bleeds. Nasal vestibulitis typically develops with extended sneezing and nose blowing such as occurs with COLDS and ALLERGIC RHINITIS. Treatment with topical and occasionally oral ANTIBIOTIC MEDICATIONS generally resolves the infection within 10 to 14 days, though symptoms should improve within 2 or 3 days. Most people experience complete recovery with no residual complications, though occasionally an ABSCESS develops that requires further medical care.

See also BLOWING THE NOSE; SNEEZE.

noise exposure and hearing Excessive exposure to noise can temporarily or permanently damage hearing. Excessive noise exposure is the most preventable cause of HEARING LOSS and accounts for as much as 60 percent of impaired hearing ability.

Several natural mechanisms attempt to protect the EAR from damage due to loud noises. The tympanic REFLEX serves to stiffen the structures of the middle ear, reducing their ability to amplify sound. In response to a loud noise, two muscles in the middle ear reflexively contract. The tensor tympani MUSCLE pulls on the malleus, and the stapedius muscle pulls on the stapes—the first and third bones, respectively, of the auditory ossicles. The effect of this reflex straightens the ossicular chain (the sequence of the ossicles), restricting the movement of the bones and dampening their ability to amplify and transfer sound waves. The ear also may experience a temporary threshold shift in response to sudden loud noises, such as gunshots and fireworks. The burst of noise appears to stun the HAIR cells, rendering them nonresponsive to sound waves in the relevant frequency range. A temporary threshold shift causes sounds to seem muffled. As long as there is no further exposure to loud noise, the hair cells gradually return to function and hearing returns to normal. However, continued or repeated exposure results in the damage becoming permanent.

Measuring Sound Volume

The unit of measure for sound volume is the decibel (dB). The decibel system is logarithmic; each increase of 10 dB represents a 10-fold increase in sound volume. A noise that measures 60 dB, such as the sound of normal conversation, is 10 times louder than a noise that measures 50 dB, such as the sound of falling rain. A clap of thunder, 120 dB, is 10 times louder than shouting directly into someone's ear, 110 dB. A rock concert (130 dB) is 10 times louder than thunder.

Most hearing experts agree that exposure to sounds louder than 85 dB begins to damage the hair cells in the COCHLEA, which activate the nerves that translate sound waves into NERVE impulses. Sounds at higher frequencies (2,000 Hz and above) do more damage at the same decibel level than sounds at lower frequencies (under 800 Hz). Much of human conversation takes place between 2,000 Hz and 4,000 Hz. Damage to the hair cells responsible for sound translation in this frequency range is particularly devastating.

Noise Exposure

Nearly everyone faces exposure to noise at levels capable of causing damage to the hair cells and ultimately hearing loss. The sounds of city traffic, a noisy restaurant, and a flushing toilet all measure in at about 85 dB. The US Occupational Safety and Health Administration (OSHA) has established regulations limiting noise exposure in the workplace. These regulations stipulate the amount of time an employee may experience noise exposure at certain decibel levels, prohibit exposure without protection to sounds over 115 dB, and prohibit exposure of any kind to sounds over 140 dB. The OSHA Web site (www.osha.gov) publishes current noise regulations and guidelines.

Musicians face the unique conundrum of needing to hear the full range of pitch while protecting their hearing from its intensity, particularly in group settings such as playing in a band or orchestra. Yet musicians playing in a rock concert may experience bursts of exposure at 150 dB, as loud as a jet taking off, which causes permanent damage to the inner ear after only a minute or two. The audience at a symphony concert experiences a sound level of 110 dB, equivalent to a car horn, and peaks near 140 dB. Musicians playing the violin, flute, and trombone face continued exposure to 110 dB or greater at frequencies above 2,000 Hz, among the most damaging of exposures. People who work in construction, steel working, mining, air travel, manufacturing, and public safety also face increased exposure to noise that threatens hearing.

Noise exposure exists in personal environments as well. Appliances such as hair dryers, blenders, coffee grinders, and even coffee makers can generate 90 dB of sound or louder. The decibel level of movies on television or in theaters can exceed 120 dB. Stereos played beyond the halfway point on the volume indicator, especially when using headphones, quickly pass the 100 dB mark. Children's noise-making toys can reach 110 dB to 140 dB.

Ear Protection

The most effective protection against noise exposure is to avoid it. As this is not always practical or possible, health experts recommend (and in the workplace OSHA requires) wearing hearing protection for exposure to sound at 90 dB for longer than eight hours and for any exposure that exceeds 90 dB. There are two kinds of ear protection: ear plugs and ear muffs.

Ear plugs fit snugly into the auditory canal and block sound waves from traveling to the middle and inner ear. They are available in various materials and in different sizes and shapes; finding ear plugs that fit properly and comfortably can take some experimentation. Custom ear plugs are also available, made specifically to fit an individual's ears. A common complaint about ear plugs is that they block so much sound that conversation is difficult. This dampening of the sound is called attenuation. Some designs of ear plugs contain channels that allow sounds at certain frequencies to pass through. This improves the ability to hear and understand speech. Customized ear plugs for musicians can block selected sounds so the musician can hear the tones and pitches necessary to play or sing.

Ear muffs fit over the ears with a strap that holds them in place. They form a seal around the ear, which prevents sound waves from traveling into the auditory canal. As with ear plugs, there are various designs that offer different levels of effectiveness and comfort. Ear muffs tend to muffle all sound, though ear muffs and ear plugs have comparable ability to block noise, about 30 dB. People exposed to noise louder than 100 dB to 110 dB should use both ear plugs and ear muffs, which in combination can block up to about 45 dB.

See also AUDIOMETRIC ASSESSMENT; COCHLEAR IMPLANT; HEARING AID; OCCUPATIONAL HEALTH AND SAFETY.

nose The facial structure that serves as the organ of smell as well as the portal through which air

enters and leaves the pulmonary system. Air enters the nose through the nostrils, passing beneath the olfactory NERVE endings. Odor molecules activate the nerve endings, which convert the stimulation into nerve signals the olfactory nerve (first cranial nerve) transmit to the BRAIN. The air then swirls through the paranasal SINUSES, cavities within the bones that form the face. The sinuses warm and moisturize the air, bringing it closer to the temperature and humidity of the inner airways. Because it extends from the face, the nose is vulnerable to traumatic injury and also to environmental exposure hazards such as FROSTBITE and SUNBURN. Numerous dermatological conditions can affect the outer nose, among them ACNE, ROSACEA, SKIN CANCER, ACTINIC KERATOSIS, and KERATOACANTHOMA. Surgery to alter the appearance of the nose, RHINOPLASTY, is one of the most common cosmetic procedures that plastic surgeons perform.

COMMON CONDITIONS AFFECTING THE STRUCTURES OF THE NOSE

ALLERGIC RHINITIS	BROKEN NOSE
EPISTAXIS	NASAL POLYP
NASAL VESTIBULITIS	RHINORRHEA
SEPTAL DEVIATION	SEPTAL PERFORATION
SINUSITIS	

For further discussion of the nose within the context of otolaryngologic structure and function please see the overview section "The Ear, Nose, Mouth, and Throat."

See also CRANIAL NERVES; MOUTH; OPERATION; THROAT.

nosebleed See EPISTAXIS.

O

obstructive sleep apnea A disorder in which blockage of the airways takes place during sleep when the structures of the neck and THROAT relax, causing BREATHING to stop for periods of time. The characteristic symptoms are a repeated pattern during sleep of loud, heavy snoring followed by a period of silence followed by gasping or snorting and tiredness during waking hours. The snoring indicates the structures of the throat are relaxing and the passage for air is narrowing; the silence indicates relaxation has reached the point at which no air is getting through. The gasping or snorting is a reflexive reaction to the drop in the blood's oxygen level; it serves to restart breathing. The cycle results in continuous interruption of sleep, leaving the person deprived of rest. The repeated episodes of oxygen deprivation can cause or contribute to numerous health problems, including HYPERTENSION (high BLOOD PRESSURE), ARRHYTHMIA (irregular heartbeat), PULMONARY HYPERTENSION, and HEART FAILURE (reduced ability of the HEART to pump BLOOD).

Many people who have obstructive sleep apnea are not aware that they do, though often their partners complain about their snoring. Often the first indication is the uncontrollable urge to fall asleep during the day, which may occur at dangerous times, such as when driving. Frequent headaches, lack of energy, and irritability are other symptoms. The diagnostic path includes a detailed sleep questionnaire and careful physical examination with a focus on the structures of the MOUTH and neck. The doctor may also request a sleep lab assessment, in which the person spends the night under observation and with electronic monitoring to objectively assess the sleep experience.

About 40 percent of people who have obstructive sleep apnea have obesity. When this is the case, WEIGHT LOSS AND WEIGHT MANAGEMENT are key to treatment. Lifestyle modifications, such as avoiding ALCOHOL or medications that cause sleepiness (such as ANTIHISTAMINE MEDICATIONS or sleep aids), can improve the body's ability to retain control over the muscles of the throat. Some people benefit from surgery to remove excess tissue at the back of the throat (uvulopalatopharyngoplasty). A continuous positive airway pressure (CPAP) device to maintain pressure against the airways and to keep them open is often an effective treatment when other approaches are not appropriate or not successful.

See also SLEEP DISORDERS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

oral hygiene Self-care methods for maintaining health of the TEETH, gums, and MOUTH. Oral healthcare providers recommend brushing the teeth at least twice daily and flossing or using an interdental device to clean between the teeth once daily. People who snack throughout the day should brush more frequently to clear away food debris and BACTERIA that accumulate after eating. Appropriate oral hygiene helps maintain the health of the teeth, gums, and other structures of the mouth and also reduces the risk of INFECTION in people who have tongue, lip, or other oral PIERCINGS. Tooth decay and gum disease develop more rapidly in people who have diminished saliva production, have DIABETES, or who smoke. Further preventive care measures include regular visits to the dentist and dental hygienist for cleaning and examination to detect oral health problems such as GINGIVITIS, PERIODONTAL DISEASE, and oral CANCER.

See also HALITOSIS; SJÖGREN'S SYNDROME; SMOKING AND HEALTH; TOBACCO USE OTHER THAN SMOKING.

otitis An INFLAMMATION of the EAR, typically the middle ear (otitis media) or the outer ear (otitis externa). Otitis can affect the inner ear (otitis interna), though more often doctors identify inner ear problems as LABYRINTHITIS and related conditions. The most common cause of otitis is INFECTION. Otitis media often follows a cold or other upper respiratory infection. Otitis can be acute (comes on suddenly) or chronic (lingers at a subclinical level or recurs).

Otitis Media

Otitis media is one of the most frequent reasons parents take their children to see the doctor. Young children are particularly susceptible to otitis media because the eustachian tubes are nearly horizontal until the child's facial structure begins to elongate at about age six or seven. The change in facial structure pulls the eustachian tubes into more angled positions. The purpose of the EUSTACHIAN TUBE is to maintain pressure equilibrium between the middle ear and the external environment. Inequities in pressure allow fluid to accumulate in the middle ear, which inflames the tissues and provides fertile ground for bacterial growth. The eustachian tubes in a child are also prone to becoming congested, which can feed fluid and BACTERIA into the middle ear.

Symptoms of otitis media are primarily PAIN and FEVER. Very young children often tug at the affected ear, are fussy and sleep fitfully, and may not want to nurse or bottle-feed. Older children can say that their ears hurt or may complain of HEADACHE. When there is a ruptured eardrum, there is usually pus-filled or blood-tinged drainage from the ear. Pain lessens when the eardrum gives way because this releases the pressure. It is not possible for a parent to determine whether a child has an ear infection; the doctor must examine the ear with an otoscope. The doctor looks for signs of effusion, the collection of fluid behind the TYMPANIC MEMBRANE (eardrum). When effusion is present, the preferred treatment is an oral antibiotic medication.

The American Academy of Pediatrics issued treatment guidelines in 2004 that emphasize selective use of ANTIBIOTIC MEDICATIONS for acute otitis media without effusion. Clinical research studies have failed to conclusively demonstrate a more rapid rate of recovery with antibiotics when there is no effusion. The treatment guidelines reflect the growing concern among health-care providers that inappropriate antibiotic use is responsible for an alarming increase in the strains of bacteria that are resistant to antibiotics. The guidelines suggest

- focusing on pain relief by giving the child appropriate doses of ibuprofen or acetaminophen
- allowing 48 to 72 hours for the child's natural immune response to bring the infection and inflammation under control
- prescribing an antibiotic as the first line of treatment only in children under six months of age or who have a history of recurrent otitis media
- prescribing amoxicillin as the antibiotic of first choice unless there is a clinical reason (such as sensitivity or known resistance) to prescribe a different antibiotic

Acute otitis media generally clears up in 10 to 14 days. Chronic or recurrent otitis media may require a more extended course of antibiotic therapy or MYRINGOTOMY with placement of tympanostomy tubes. Adenoidectomy (surgery to remove the ADENOIDS) may be necessary when other measures fail to eradicate the infection. Many children experience temporary HEARING LOSS with otitis media. Repeated infections may cause permanent hearing damage.

Otitis Externa

A common name for otitis externa is swimmer's ear. Infections of the outer ear are most common in the summer months when water activities, especially outdoors, are prevalent. Otitis externa develops when water and bacteria become trapped in the auditory canal. Sometimes excessive CERUMEN production contributes to the situation. Treatment depends on the cause of the inflammation and irritation. Taking care to thoroughly dry the auditory canals after bathing, showering, or swimming can help prevent otitis externa.

See also ANTIBIOTIC RESISTANCE; OTORRHEA.

otoplasty Surgery to alter the appearance of the auricle (external EAR). Otoplasty can be cosmetic (to improve appearance) or restorative (to treat congenital deformities or those that result from trauma and BURNS). The auricle is primarily CARTILAGE and SKIN; the cartilage gives the external ear its shape and position on the side of the head. Numerous causes account for abnormalities. Otoplasty can remodel the cartilage to alter the size, shape, and placement of the auricle and even reconstruct an auricle that is missing or severely deformed.

See also CAULIFLOWER EAR; PIERCINGS; PLASTIC SURGERY.

otorrhea A discharge from the EAR. Most commonly otorrhea signals the presence of OTITIS, an INFECTION of the outer ear (otitis externa) or the middle ear (otitis media). Otorrhea is normal after MYRINGOTOMY and placement of tympanostomy tubes, as the purpose of these procedures is to drain accumulated fluid from the middle ear. Drainage that is yellowish green typically contains pus. Red-tinged discharge contains BLOOD. Either of these may indicate otitis media with a perforated TYMPANIC MEMBRANE (RUPTURED EARDRUM). Drainage that is yellowish brown and thick may be excessive CERUMEN, often in response to the ear's attempts to clear matter from the auditory canal or to soothe irritated tissues.

Bright bleeding or drainage from the ear that is watery and clear requires emergency medical attention.

Trauma to the head, such as from a blow or a fall, can cause outright bleeding from the ear and may indicate a BONE FRACTURE. Trauma also can cause CEREBROSPINAL FLUID to leak into the middle ear and drain from the outer ear when a perforation allows the fluid to pass from the middle ear to the outer ear or from the NOSE (RHINORRHEA) when the tympanic membrane is intact. Drainage of cerebrospinal fluid also sometimes occurs following surgery to remove an ACOUSTIC NEUROMA; in any other circumstance it may indicate MENINGITIS.

Treatment targets the underlying cause. ANTIBIOTIC MEDICATIONS are necessary when otitis is responsible. Other conditions such as DERMATITIS of the auditory canal may improve with topical CORTICOSTEROID MEDICATIONS. When the drainage is cerumen, gently rinsing the ears with warm water during bathing helps remove the excess.

See also CLEANING THE EAR; FOREIGN OBJECTS IN THE EAR OR NOSE.

otosclerosis Abnormal growth of BONE tissue around the auditory ossicles in the middle EAR, causing one or more of the ossicles to become locked into place or fused against the other ossicles. Most commonly affected is the stapes (stirrup), the final of the three auditory ossicles in the sequence of sound wave amplification and transmittal. Conductive HEARING LOSS, which is the primary symptom of otosclerosis, occurs as movement of the auditory ossicles becomes increasingly limited. Occasionally otosclerosis involves the COCHLEA, causing sensorineural hearing loss and sometimes vestibular dysfunction such as balance disturbances and VERTIGO.

An AUDIOLOGIC ASSESSMENT identifies the hearing loss. The otolaryngologist may request a COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to visualize the structures of the inner ear and to confirm the diagnosis. Surgical treatments often can restore conductive hearing loss to near normal hearing. An OPERATION to remove the immobilized ossicle and replace it with a prosthetic ossicle can permanently restore hearing in most people. Surgery is less successful in restoring hearing loss due to cochlear otosclerosis, though a HEARING AID often can improve hearing.

See also SURGERY BENEFIT AND RISK ASSESSMENT; TINNITUS.

otoscopy A basic visual examination of the outer and middle EAR using an otoscope, a handheld, lighted device with a magnifying lens. The otoscope has cone-shaped tips in varying sizes that fit into the start of the auditory canal. With an otoscope, the doctor can examine the auditory canal for injury, INFLAMMATION, INFECTION (OTITIS externa) blockages such as foreign objects or compacted CERUMEN, and structural deformities. The doctor also can visualize the outer surface of the TYMPANIC MEMBRANE for inflammation, infection,

OTOTOXIC MEDICATIONS

Medications	Commonly Prescribed to Treat	Ototoxic Effects
ANGIOTENSIN-CONVERTING ENZYME (ACE) inhibitors: enalapril, lisinopril, ramipril, quinapril, trandolapril	HYPERTENSION	TINNITUS, HEARING LOSS usually temporary, reversible when medication stopped
aminoglycoside antibiotics: amikacin, gentamicin, kantamycin, neomycin, streptomycin. tobramycin	in intravenous form: *Acinetobacter, Enterobacter, Pseudomonas,* and *Mycobacter* infections in topical form: ear drops following myringotomy	hearing loss, balance disturbances some degree of loss is often permanent; risk increases when also taking any other medications with ototoxic effects
aspirin (salicylic acid)	PAIN, INFLAMMATION, mild anticoagulant	tinnitus, hearing loss with high doses, balance disturbances usually temporary, reversible when medication stopped
platinum-derived CHEMOTHERAPY agents: carboplatin, cisplatin	certain cancers (BLADDER, LUNG, ovarian STOMACH, testicular)	moderate to severe hearing loss usually permanent
loop diuretics: bumetanide, ethacrynic acid, furosemide, torsemide	hypertension, congestive heart failure, KIDNEY disease	tinnitus, hearing loss usually temporary, reversible when medication stopped
macrolide antibiotics: azythromycin, clarithromycin, erythromycin	*Helicobacter pylori* infection (PEPTIC ULCER DISEASE), *Legionella* PNEUMONIA (LEGIONNAIRES' DISEASE), alternative when when there are allergies to penicillin and cephalosporin antibiotics	hearing loss, sometimes severe usually temporary, reversible when medication stopped
NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS): over the counter (OTC): ibuprofen, naproxen sodium, ketoprofen prescription: oxaprozin, diclofenic, etodolac, meloxicam, celecoxib,	pain, inflammation, arthritis	tinnitus, mild to moderate hearing loss, balance disturbances usually temporary, reversible when medication stopped
bismuth subsalicylate (for example, Pepto-Bismol)	gastrointestinal upset, DIARRHEA	tinnitus, mild to moderate hearing loss, balance disturbances usually temporary, reversible when medication stopped
quinine, chloroquine, quinidine	MALARIA, arrhythmias, leg cramps	tinnitus, mild to moderate hearing loss, balance disturbances, vertigo usually temporary, reversible when medication stopped

perforation, deformities, movement, and signs of increased pressure in the middle ear such as bulging or fluid that suggests otitis media (middle ear infection). Otoscopy is the primary diagnostic procedure for many conditions affecting the outer ear, and the first step of the diagnostic path for conditions affecting the middle ear. Otoscopy cannot determine hearing ability or HEARING LOSS.

See also AUDIOLOGIC ASSESSMENT; MYRINGITIS; RUPTURED EARDRUM.

ototoxicity A medication SIDE EFFECT that results in damage to the functions and structures of the EAR and hearing. The damage can be temporary, in which case symptoms recede and hearing returns when the person stops taking the medication, or permanent. Numerous medications can be ototoxic at therapeutic doses, making it prudent to weigh this potential consequence against the anticipated benefits of the medication. Often medication options are available that can achieve the desired therapeutic effect without the risk for ototoxicity.

Symptoms of ototoxicity include

- TINNITUS (sensation of ringing or rushing sound)
- indications of HEARING LOSS, such as difficulty understanding conversation or being unable to hear the telephone ring
- balance disturbances and dizziness
- VERTIGO (sensation of spinning)

Report any of these symptoms to the doctor immediately, though do not stop taking any medications until discussing the circumstances with him or her. Most ototoxic medications appear to act on the delicate HAIR cells in the COCHLEA, stunning or destroying their ability to translate sound waves into NERVE signals. Ototoxicity is most devastating when it affects high-frequency hearing, the range of normal conversation.

Numerous industrial chemicals are also ototoxic. They include butyl nitrite, carbon disulfide, hexane, manganese, lead, mercury, styrene, and toluene. Hearing loss resulting from exposure to these chemicals is often permanent.

See also AUDIOLOGIC ASSESSMENT; NOISE EXPOSURE AND HEARING; OCCUPATIONAL HEALTH AND SAFETY; TOXIC OPTIC NEUROPATHY.

P

periodontal disease Inflammatory and sometimes infectious damage to the gums. Periodontal disease causes gum tissue to recede from the TEETH, which allows teeth to loosen. It also exposes the less protected area of the tooth to BACTERIA that cause tooth decay, resulting in DENTAL CARIES (cavities) and potential INFECTION such as ABSCESS of the root canal. Periodontal disease is the leading cause of tooth loss in adults. Dental care providers estimate that up to 60 percent of American adults have some degree of periodontal disease.

Symptoms of periodontal disease include

- painless bleeding, especially when brushing the teeth
- swollen, shiny, or red gums
- gaps between the gums and the teeth
- loose teeth
- HALITOSIS (bad breath) that does not improve with brushing or mouthwash

Dentists provide diagnosis and treatment for periodontal disease. Appropriate ORAL HYGIENE can prevent most periodontal disease; identifying periodontal disease early allows opportunity for therapeutic interventions to thwart permanent damage. Some health experts believe there are connections between the body's inflammatory response, periodontal disease, and other health conditions such as ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD).

See also GINGIVITIS; INFLAMMATION.

peritonsillar abscess A serious and painful INFECTION of the tissues around the tonsils in the back of the THROAT. Unlike TONSILLITIS, which is primarily an infection among children, peritonsillar ABSCESS is most common among adults in early midlife. Doctors are uncertain what causes a peritonsillar abscess to develop, though it will often follow another infection such as tonsillitis, PHARYNGITIS or mononucleosis.

Symptoms emerge suddenly. They include

- severe and usually one-sided PAIN in the throat
- pain in the EAR on the opposite side from the abscess with swallowing
- FEVER
- a whispery, hoarse voice
- neck stiffness and sometimes swelling on the front of the neck
- difficulty swallowing
- inability to fully open the mouth (called trismus)

Symptoms and physical examination typically make the diagnosis, though the doctor may perform a laryngoscopy to more closely examine the throat. After swabbing the peritonsillar area for culture, treatment with intravenous ANTIBIOTIC MEDICATIONS begins. The person remains hospitalized until the swelling goes down and the pain abates, at which point antibiotic therapy shifts to oral doses for the remainder of treatment at home. When the abscess is large or has the potential to interfere with BREATHING, the doctor may choose to surgically open and drain it (under anesthesia). This provides dramatic relief. Most people recover fully and without complications in about two weeks.

See also ENDOSCOPY; EPIGLOTTITIS; MONONUCLEOSIS, INFECTIOUS.

pharyngitis INFLAMMATION and irritation of the pharynx (the top part of the THROAT), often due to viral or bacterial INFECTION. Seasonal allergies, environmental irritants such as smoke, and uncontrolled GASTROESOPHAGEAL REFLUX DISORDER (GERD) are also common causes of pharyngitis, often called sore throat.

Pharyngitis that interferes with BREATHING or swallowing requires emergency medical care.

Many pathogens can cause infections. Doctors estimate that viruses cause about 60 percent of pharyngitis and BACTERIA cause about 30 percent. Distinguishing the responsible PATHOGEN guides treatment, as bacterial pharyngitis requires treatment with ANTIBIOTIC MEDICATIONS. It is difficult to determine the cause of pharyngitis on the basis of symptoms. The only conclusive diagnostic measure is a throat culture to identify what pathogens are present.

The primary symptom of pharyngitis is a scratchy or sore throat. Other symptoms may occur, depending on the cause, such as FEVER, HEADACHE, COUGH, and SNEEZE. Most viral pharyngitis runs its course in 7 to 10 days. Bacterial pharyngitis greatly improves within 2 days of initiating antibiotic therapy, though it is essential to take the antibiotic medication until it is gone. Reducing or eliminating exposure to irritants such as cigarette smoke and pollen helps with noninfectious pharyngitis. A doctor should evaluate acute pharyngitis (pharyngitis that comes on suddenly) that continues longer than 10 days, and chronic pharyngitis (ongoing or recurrent) on a regular basis. Chronic pharyngitis can signal other health problems, such as laryngeal CANCER.

See also ALLERGIC RHINITIS; LARYNGITIS; POSTNASAL DRIP; SINUSITIS; SMOKING AND HEALTH; STREP THROAT.

postnasal drip Mucus from the NOSE that flows down the back of the THROAT. Postnasal drip is a common complaint and may accompany various health conditions, including COLDS, ALLERGIC RHINITIS, SINUSITIS, and OTITIS media. Postnasal drip is a common cause of PHARYNGITIS because it irritates the tissues at the back of the throat (pharynx) and can cause COUGH, especially when lying down or asleep. Swallowed postnasal drip often causes NAUSEA.

Mucus production is the body's natural mechanism for removing pathogens and debris from the nasal passages, and it is normal for it to increase as a protective measure when there is irritation to the nasal passages. Treatment focuses on identifying the underlying cause of continued excessive production. ANTIBIOTIC MEDICATIONS are helpful only when the cause is bacterial INFECTION. Medications to reduce INFLAMMATION in the nasal passages, such as oral ANTIHISTAMINE MEDICATIONS or nasal sprays, can help reduce mucus production; however, overuse of nasal sprays results in rebound congestion (increased mucus production when not using the spray). Drinking plenty of fluids helps keep mucus thin, making it easier for the body to expel. Humidified air may reduce irritation to the nasal passages to slow mucus production.

See also BACTERIA; BLOWING THE NOSE; FOREIGN OBJECTS IN THE EAR OR NOSE; RHINORRHEA; SNEEZE.

presbycusis The natural diminishment of hearing ability that occurs with aging. HEARING LOSS affects both ears, is sensorineural, and progresses in a predictable pattern, beginning with sounds in the high frequency range (2,000 Hz to 4,000 Hz). Researchers do not know the precise mechanisms through which presbycusis takes place, though most believe it occurs through a cumulative loss of cells from the inner EAR, the NERVE pathways to the BRAIN, and within the brain itself. Many factors influence the rate of progression. One third of adults between age 65 and 74 and half of those beyond age 74 have age-related hearing loss. Health conditions that affect blood circulation and nerve function, such as ATHEROSCLEROSIS and DIABETES, intensify the effects of age-related changes. Noise exposure can exacerbate the rate and nature of hearing loss. Older adults also are more likely to take medications that have ototoxic side effects, such as loop diuretics and certain antihypertensive medications.

Early indications of presbycusis, which may become apparent when a person is in his or her late 50s or early 60s, include difficulty hearing

certain sounds and words, because the frequency range that is lost is that of conversation. Turning up the volume on the television and perceptions that other people are mumbling are also signs of hearing loss. There are no known methods for preventing presbycusis. Hearing aids often improve hearing ability, though the progressive loss of hearing may eventually exceed the capability of the HEARING AID.

See also AGING, OTOLARYNGOLOGIC CHANGES THAT OCCUR WITH; NOISE EXPOSURE AND HEARING; OTOTOXICITY; PRESBYOPIA.

R

rhinoplasty Plastic surgery to repair or reconstruct the NOSE. Surgeons perform rhinoplasty operations for cosmetic and for reconstructive reasons. Cosmetic rhinoplasty is the most commonly performed PLASTIC SURGERY procedure in the United States, with more than 350,000 operations each year. Reconstructive rhinoplasty helps restore the function and appearance of the nose when there are structural defects such as SEPTAL DEVIATION or following serious trauma (such as a BROKEN NOSE) and conditions such as SKIN CANCER or other cancers affecting the nose.

Rhinoplasty is nearly always an AMBULATORY SURGERY performed under general or local ANESTHESIA. The surgeon may reshape the CARTILAGE and occasionally the BONE. Swelling and discoloration are common following the OPERATION, gradually diminishing over two to three weeks. Bleeding and INFECTION are among the potential risks of rhinoplasty. Because the nose has an abundant blood supply, surgeons typically insert compression packing into the nose for one to three days after surgery, which applies pressure to minimize bleeding and maintain the integrity of the reshaping. The packing carries a risk of TOXIC SHOCK SYNDROME, a serious systemic bacterial infection. The surgeon should promptly evaluate any FEVER or increase in PAIN.

As with any surgery, the results of rhinoplasty can vary. It is important to understand the limitations and consequences of the operation and to have realistic expectations for cosmetic results. Reconstructive rhinoplasty may require several operations to achieve the desired outcome. Most people can return to their regular activities within two weeks.

See also BLEPHAROPLASTY; OTOPLASTY; RHYTIDOPLASTY; SURGERY BENEFIT AND RISK ASSESSMENT.

rhinorrhea The medical term for runny NOSE. Mucus discharge from the nose is the body's mechanism for removing foreign matter. Numerous factors can cause rhinorrhea. Among the most common are exposure to allergens, such as pollen and dust, and INFECTION, such as COLDS, SINUSITIS, OTITIS, and PHARYNGITIS. In young children, foreign objects in the nose also commonly cause rhinorrhea. Discharge that contains pus or blood suggests infection.

Clear, watery nasal drainage following head trauma requires immediate medical attention as this may indicate that CEREBROSPINAL FLUID is leaking.

Rebound rhinorrhea can develop with excessive use of nasal sprays as well as oral decongestants and ANTIHISTAMINE MEDICATIONS. When the doctor can identify the underlying cause, treatment targets that cause. Otherwise, treatment targets relief of symptoms. Topical decongestants (nasal sprays) are the treatment of first choice, applied for a short and defined period of time. The doctor may also recommend oral decongestants or antihistamines.

See also BLOWING THE NOSE; EPISTAXIS; FOREIGN OBJECTS IN THE EAR OR NOSE; SNEEZE/COUGH ETIQUETTE.

ruptured eardrum A tear in the TYMPANIC MEMBRANE, or eardrum, that results from trauma of some kind. The primary symptoms are

- sudden and sharp PAIN from the EAR
- drainage (when the cause is INFECTION)
- TINNITUS (a ringing or roaring sound)

- HEARING LOSS in the affected ear

A tear in the tympanic membrane causes it to lose tension, which affects hearing as the breach affects the eardrum's ability to vibrate. When infection (OTITIS media) causes the rupture, the pain of the tear is followed by relief of pain because the tear releases the fluid that has accumulated in the middle ear behind the tympanic membrane. Other common causes of ruptured eardrum include

- exposure to a sudden, loud noise
- BAROTRAUMA (damage from rapid and extreme changes in pressure)
- puncture from a foreign object inserted into the ear, such as a cotton swab or hair pin (bobby pin) being used to clean CERUMEN (ear wax) from the auditory canal

The doctor's otoscopic examination of the ear, which allows visualization of the tympanic membrane, confirms the diagnosis. Most ruptured eardrums heal without intervention in about six weeks, with hearing gradually improving as the tympanic membrane regains integrity and tension. For a large tear, the otolaryngologist may put a small paper patch over the opening to help protect the inner ear while the tear heals or may perform an OPERATION (TYMPANOPLASTY) to repair the damaged eardrum. Earplugs are necessary during bathing or showering to keep water from entering the auditory canal during the time the tear is HEALING. Hearing typically returns when the tear heals. A potentially significant consequence of ruptured eardrum is formation of a CHOLESTEATOMA, a cystlike growth in the inner ear that can permanently damage hearing.

See also MYRINGITIS; MYRINGOTOMY; OTOSCOPY.

S

salivary glands Structures within the MOUTH that produce saliva, a watery fluid that mixes with food during chewing and maintains the mouth as a moist environment. The major salivary glands are primarily along the floor of the mouth (the sublingual and submandibular glands) and at the back of the mouth just below the EAR (parotid glands). These glands produce a steady supply of saliva that trickles into the mouth to moisturize mucous membranes. Stimuli related to eating, such as the smell or appearance of food, activate an increased flow of saliva to meet the needs of mastication (chewing). Enzymes in saliva begin to break down foods to prepare them for digestion.

The facial and glossopharyngeal nerves, the seventh and ninth CRANIAL NERVES respectively, regulate the functions of the salivary glands. The glossopharyngeal NERVE also handles nerve impulses for the sense of taste. Small mineral calculi, or stones, can block the salivary ducts that drain saliva from the salivary glands, causing PAIN and swelling (SIALOLITHIASIS). Excessive saliva (SIALORRHEA), or drooling, can a symptom of various neurologic conditions, including CEREBRAL PALSY and PARKINSON'S DISEASE, and often accompanies SWALLOWING DISORDERS. Saliva production temporarily increases in young children who are teething, likely an attempt by the body to soothe the discomfort of the new TEETH erupting through the surface of the gums. The parotid glands swell with the MUMPS.

For further discussion of the salivary glands within the context of otolaryngologic structure and function please see the overview section "The Ear, Nose, Throat, and Mouth."

See also SIALADENITIS.

septal deviation A shift from midline in the nasal septum (wall of tissue that separates the air pathways of the NOSE). Septal deviation can cause various health conditions such as chronic SINUSITIS (INFECTION), EPISTAXIS (nosebleed), and obstructed BREATHING. It can occur as a natural defect or result from trauma such as a blow to the nose. The treatment of choice is surgical correction (septoplasty) to restore the septum to midline. Septal deviation often accompanies structural anomalies of the nose that cause people to seek RHINOPLASTY (surgical reconstruction of the nose).

See also SEPTAL PERFORATION; SURGERY BENEFIT AND RISK ASSESSMENT.

septal perforation An abnormal opening in the nasal septum (wall of tissue within the NOSE that divides the nostrils), that occurs as the result of chronic irritation, trauma, or cancer. Septal perforation may develop with long-term use of nasal oxygen, long-term use of corticosteroid nasal sprays (such as to treat ALLERGIC RHINITIS), inhalation of illicit drugs such as COCAINE or aerosols and glues, foreign objects in the nose, chronic digital trauma (picking the nose), or long-term exposure to chromates such as chromic acid and chromium (used in electroplating and other industrial applications). Septal perforation sometimes occurs as a consequence of RHINOPLASTY, particularly when there have been several operations.

Symptoms of septal perforation may include a whistling sound when BREATHING, nasal discharge, and bleeding (EPISTAXIS). The preferred treatment for most septal perforations is surgical repair (septoplasty), though it is sometimes necessary to first remedy the underlying cause. The doctor may place a nasal septal prosthesis, commonly called a

nasal button, that fits into the perforation to create a temporary closure. Untreated septal perforation results in frequent infections and continued erosion of the nasal lining as well as CARTILAGE.

See also FOREIGN OBJECTS IN THE EAR OR NOSE; OCCUPATIONAL HEALTH AND SAFETY; RHINORRHEA; SURGERY BENEFIT AND RISK ASSESSMENT.

sialadenitis INFLAMMATION and swelling of a salivary gland, usually a submandibular or parotid gland. Common causes include

- SIALOLITHIASIS, in which a small "stone" or mineral calculus blocks the flow of saliva and irritates the tissues of the involved salivary gland
- bacterial INFECTION, which can develop when the blockage persists because the MOUTH contains an abundance of BACTERIA
- viral infection with various viruses, including MUMPS, coxsackie, INFLUENZA, herpes, and human immunodeficiency virus (HIV)
- AUTOIMMUNE DISORDERS such as SJÖGREN'S SYNDROME and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Diagnosis arises mostly through physical examination and other clinical indicators, though sometimes the doctor will order X-rays or other imaging procedures to help distinguish the cause or to determine whether an ABSCESS (pocket of infection) is present. Treatment focuses on the underlying cause of the inflammation. Bacterial sialadenitis requires treatment with ANTIBIOTIC MEDICATIONS. Antibiotics are not helpful for viral sialadenitis, which typically improves in 10 to 14 days. Regardless of cause, drinking plenty of fluids, frequently rinsing the mouth with warm saltwater or applying warm compresses (moist heat) to the outside of the face over the affected area, and taking a nonsteroidal anti-inflammatory drug (NSAID) such as ibuprofen can help relieve discomfort.

See also BACTERIA; HIV/AIDS; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); VIRUS; X-RAY.

sialolithiasis The formation of a crystallized mineral deposit, called a salivary calculus ("stone"), in a salivary gland. Sialolithiasis most commonly involves the submandibular and parotid SALIVARY GLANDS. Its primary symptoms are PAIN and swelling when it blocks the flow of saliva from the gland. Sometimes the calculus remains symptomless and undetected until it shows up on an X-RAY done for other reasons such as a routine dental exam. Doctors sometimes use COMPUTED TOMOGRAPHY (CT) SCAN, ULTRASOUND, or sialography to confirm the diagnosis. A small calculus may pass from the gland on its own. Because the risk of INFECTION is high, however, doctors prefer to surgically remove salivary calculi. The OPERATION involves making a small incision into the salivary gland and extracting the calculus. Recovery is usually complete, though some people have recurrent episodes or experience narrowing (stricture) of the affected salivary duct. Researchers do not know what causes salivary calculi to develop.

See also SIALADENITIS; SURGERY BENEFIT AND RISK ASSESSMENT.

sialorrhea Excessive saliva production that may result in drooling or choking if there are impairments to swallowing. Sialorrhea often accompanies neurologic disorders and BRAIN injuries that affect the parasympathetic NERVOUS SYSTEM, which regulates the functions of most of the body's glands. People who have sialorrhea are at risk for ASPIRATION (inhaling excessive saliva into the airways and LUNGS), choking, INFECTION, and irritation of the SKIN around the face and neck. Sialorrhea also presents significant hygienic concerns and often is embarrassing to the person who has it.

Anticholinergic medications, which "dry out" the body, curtail sialorrhea in many people. These medications also affect neurotransmitters in the brain, however, which can have unintended detrimental effects on motor function. Some people benefit from botulinum toxin A injections (BOTULINUM THERAPY) into the tissues surrounding the salivary glands, which temporarily paralyzes the muscles that release saliva. Other treatment approaches include surgery to remove or obstruct portions of the submandibular salivary glands, which produce about 80 percent of the saliva, and therapy to improve muscle control and swallowing ability. Treatment success depends on the underlying causes.

See also NEUROTRANSMITTER; SIALADENITIS; SIALOLITHIASIS.

sign language A nonverbal language that serves as a system of communication for people who are hearing impaired. Sign language uses hand signals to represent letters of the alphabet and gestures to represent words, phrases, and concepts. As in spoken languages, sign languages incorporate an extensive vocabulary with rules that govern its presentation (grammar and syntax). The sign languages most used in the United States are

- American Sign Language (ASL) derives its structure from French Sign Language, which was the first formal sign language, and is a unique language separate from spoken English. ASL is the third most common language in the United States.
- Signing Exact English (SEE) evolved in the early 1970s as a method to manually code spoken English for children learning to read and for people without hearing impairment who communicate with those who have hearing impairment.
- Pidgin Signed English (PSE) blends aspects of ASL and SEE for colloquial or casual communication.

Though sign languages may carry a culture's name, such as American Sign Language or Japanese Sign Language, there is no correlation between the sign language and the culture's spoken language. Nor are sign languages necessarily similar to each other.

The BRAIN processes sign languages differently from spoken languages. Because spoken languages form the basis for reading and writing, prelingual children who have profound HEARING LOSS may easily learn a sign language and yet have difficulty learning to read and write.

See also BRAILLE; COGNITIVE FUNCTION AND DYSFUNCTION.

sinuses Cavities within the facial bones around the NOSE, also called the paranasal sinuses, that warm and moisten inhaled air. Mucous membrane lines the sinuses, providing a continuous supply of moisture. Mucus production increases in response to irritation, for example, from environmental particles (pollen, smoke), viruses, and BACTERIA. The maxillary sinuses, on the face along the ridge of BONE commonly called the cheek bone, and the frontal sinuses, above the inside corners of the eyes near the bridge of the nose, are the sinuses that most commonly become congested as a result of COLDS, allergies, and infections. The sinuses also function as sound chambers that give the voice resonance and amplification. Sinus congestion limits this function, resulting in a characteristic "nasal" voice.

For further discussion of the sinuses within the context of otolaryngologic structure and function please see the overview section "The Ear, Nose, Mouth, and Throat."

See also ALLERGIC RHINITIS; NASAL POLYP; SINUSITIS.

sinusitis INFLAMMATION of the SINUSES. The most common causes of sinusitis are INFECTION and environmental irritation such as seasonal allergies (ALLERGIC RHINITIS). Sinusitis affects an estimated 37 million Americans each year. It can be acute (lasts a few weeks), chronic (lasts months to years), or recurrent (occurs in repeated acute episodes). Doctors further define chronic sinusitis by the extent of permanent damage to the mucous lining of the nasal passages. Long-term chronic sinusitis causes narrowing of the openings through which mucus drains out of the sinuses.

Symptoms and Diagnostic Path

The symptoms of sinusitis include

- PAIN across the cheek bones or between the eyes
- pain in the upper jaw and TEETH
- persistent HEADACHE that is worst on awakening in the morning and improves through the day though does not entirely go away
- nasal congestion
- frequent sneezing
- thick, colored discharge from the nostrils
- POSTNASAL DRIP

Some people with sinusitis also have FEVER, COUGH, and PHARYNGITIS (from the postnasal drip). The diagnostic path includes careful examination of the inside of the NOSE. For acute sinusitis the doctor may make the diagnosis on the basis of what he or she observes. Doctors seldom order

regular X-rays, once the standard of diagnosis, because the results are not reliable. For chronic sinusitis the otolaryngologist conducts an extensive examination that includes a COMPUTED TOMOGRAPHY (CT) SCAN and ENDOSCOPY to directly evaluate the condition of the sinuses. The doctor may also culture a sample of the nasal discharge to identify the BACTERIA that are present.

Treatment Options and Outlook

Acute bacterial sinusitis requires to treatment with an ANTIBIOTIC MEDICATIONS. Decongestant medications help relieve stuffiness and congestion by constricting the blood vessels that supply the mucous tissue within the nose. ANTIHISTAMINE MEDICATIONS mitigate the body's immune response to allergens such as dust and pollen that cause local irritation of the nasal tissues.

Chronic bacterial sinusitis often requires irrigation of the sinuses with a solution of antibiotic and decongestant, which the otolaryngologist does as an office procedure. Home treatment may include an oral antibiotic, humidifier to add moisture to the air, and saline nose drops to keep the nasal passages moist. Moisture helps reduce irritation and swelling. Surgery may be necessary to correct any problems such as septal defect, SEPTAL PERFORATION, and NASAL POLYP, or to widen the nasal ostia (openings in the sinuses).

Risk Factors and Preventive Measures

Sinusitis is more common in people who have seasonal rhinitis (allergies). The presence of allergens causes the nasal passages to swell, establishing ideal conditions for bacteria to grow. Keeping seasonal rhinitis symptoms under control helps reduce congestion. Sinusitis is also more common in people with structural anomalies of the nose such as SEPTAL DEVIATION. Untreated, chronic, or recurrent OTITIS media (ear infection) can funnel bacteria to the base of the nose via the EUSTACHIAN TUBE. Prompt, appropriate treatment for acute sinusitis helps limit recurrent and chronic infections.

See also ALLERGEN; SNEEZE; X-RAY.

smell and taste disturbances Dysfunctions of smell and taste result in the inability to perceive odors and tastes or the BRAIN interpreting smell and taste messages incorrectly. Dysfunctions that affect the perceptions of smell and taste are common side effects of medications, consequences of health conditions such as STROKE, and dimensions of aging. Disturbances of smell and taste affect one's ability to enjoy daily pleasures such as the fragrances of flowers and the flavors of foods. But smell and taste are not only matters of QUALITY OF LIFE. These chemosenses, as researchers refer to them, also provide early warning of potentially hazardous circumstances. Many spoiled foods, for example, smell and taste rancid. In the United States, natural gas distributors add the chemical mercaptan, which smells strongly like rotten eggs, to pipelines and storage tanks to warn of gas leaks.

Because the functions and disturbances of smell and taste are nearly inseparable, disturbances of one affect the other. Most commonly, diminished smell reduces the ability to perceive flavors. Though the taste cells within the taste buds may remain fully functional, the brain requires the detailed NERVE signals the olfactory bulb gathers and sends to interpret flavors. The brain perceives primarily bitterness when taste is the only sense sending messages about chocolate, for example, because cocoa, chocolate's key ingredient, is a bitter substance. The brain interprets the distinctive sweetness and flavor of chocolate only when the olfactory sensors detect and report the hundreds of odor molecules that chewing releases from the chocolate, which then swarm into the NOSE from the back of the THROAT. As much as 80 percent of the perception of flavor derives from smell.

Symptoms and Diagnostic Path

Though about 200,000 Americans seek medical care for disturbances of taste and smell, health experts believe millions live with diminished or altered chemosenses without realizing it. People are most likely to notice disturbances that come on suddenly or involve distinctive changes. Most people report problems with taste, though typically the culprit is more often related to smell. Symptoms can range from isolated to total loss of smell, taste, or both. People may notice they no longer taste the seasonings in foods or smell the flowers in a garden. With some health conditions such as PARKINSON'S DISEASE, perceptions of flavor change. People who have DIABETES or HYPERTENSION

often experience general reductions in chemosensory perceptions.

Physical obstructions The most common cause of taste and smell disturbances is congestion, which blocks contact between odor molecules and odor sensors in the nose. Congestion results from a wide range of circumstances, most of which are temporary or transient (come and go). These include COLDS, ALLERGIC RHINITIS (seasonal allergies), and SINUSITIS. Mechanical obstructions such as nasal polyps or SEPTAL DEVIATION alter the flow of air through the nose so that odor molecules pass by only a small section of the olfactory epithelium, the patch of nerve endings extending from the olfactory bulb. Dental problems that cause irritation in the MOUTH, especially of the tongue, can disrupt the functions of taste cells.

Aging The aging process is the second-leading cause of diminished taste and smell. Researchers estimate that diminished chemosensory perception affects more than half of people over age 65; by age 80 the loss is significant enough to interfere with the desire to eat. The olfactory epithelium in the nose loses about 1 percent of its nerve cells each year. Though the tongue renews taste buds every few weeks throughout most of life, the rate of replacement slows in the later decades. By age 80, the number of taste cells in the mouth has diminished by as much as 40 percent. In combination with the loss of olfactory nerve endings, there often is the perception of complete inability to perceive flavors.

Health conditions and medication side effects

Many health conditions can cause disturbances of smell and taste. Among those most frequently implicated are diabetes, hypertension, SARCOIDOSIS, BELL'S PALSY, Parkinson's disease, ALZHEIMER'S DISEASE, and MULTIPLE SCLEROSIS. Olfactory auras (perceptions of smells) often precede migraine headaches and epileptic seizures. Numerous medications affect taste and smell, notably ANTIBIOTIC MEDICATIONS, levodopa (to treat Parkinson's disease), angiotensin-converting enzyme (ACE) inhibitors (antihypertensive medications), "statin" lipid-lowering medications, and CHEMOTHERAPY agents such as cisplatin and methotrexate. Taste and smell usually return to normal after stopping the medication, though chemotherapy-related changes may persist or become permanent. RADIATION THERAPY to the head or neck also alters chemosensory perception, often permanently.

Nerve damage Smell and taste disturbances can result from damage to the nerves that carry chemosensory messages to the brain, such as might occur with injury or neurologic diseases. The first cranial nerve (olfactory nerve) carries most odor messages to the brain, with the fifth cranial nerve (trigeminal nerve) conveying limited signals. Three CRANIAL NERVES—the seventh (facial nerve), ninth (glossopharyngeal nerve), and tenth (vagus nerve)—convey taste messages to the brain. Trauma such as from a BROKEN NOSE can damage the olfactory nerve endings in the roof of the nose. Chronic exposure to cigarette smoke or inhaled drugs (notably cocaine as well as corticosteroid nasal sprays used to treat ASTHMA and allergic rhinitis) also damages these hairlike structures.

Treatment Options and Outlook

Treatment for smell and taste disorders targets the underlying causes of the disturbances to the extent doctors can identify them. Approaches include

- reducing exposure to environmental irritants such as cigarette smoke and allergens
- treating chronic sinusitis, dental disease, and allergic rhinitis
- removing nasal polyps and correcting septal defects in the nose
- evaluating regular medications being taken to identify any that can interfere with smell and taste
- looking for patterns of chemosensory disturbance

Often, idiopathic taste and smell disturbances (those of undetermined cause) improve on their own over time. Changes due to diseases tend to follow the course of the underlying condition, progressively worsening along with the principal condition, as in Parkinson's disease or multiple sclerosis.

Risk Factors and Preventive Measures

Treating infections promptly and avoiding irritants that interfere with olfactory and gustatory func-

tions are the most effective measures for protecting the chemosenses. Subclinical sinusitis (ongoing sinus infection that does not have symptoms), structural defects of the nose (such as nasal polyps and septal deviation), and allergic rhinitis are the most common causes of disturbances involving these senses. Most are correctable, which nearly always restores smell and taste. Other efforts include reducing exposure to cigarette smoke, industrial pollutants, and inhaled drugs such as cocaine. Unfortunately age-related diminishment is permanent. Most people with smell and taste disturbances can learn methods to accommodate the diminished perception of flavor with seasonings (other than salt and sugar) to enhance foods and beverages.

See also AGING, OTOLARYNGOLOGICAL CHANGES THAT OCCUR WITH; NASAL POLYP; SJÖGREN'S SYNDROME; SMOKING AND HEALTH.

sneeze A REFLEX that forcefully expels air through the NOSE. A sneeze originates with an irritation to the mucous membranes in the nose, sometimes perceptible as a tickling sensation and other times not noticeable, that activates NERVE impulses. The fifth cranial nerve (trigeminal nerve) carries the impulse to a cluster of specialized neurons (nerve cells) in the brainstem (the part of the BRAIN that regulates the body's basic vital functions including reflexes). Scientists call this area the sneeze center, though they do not know its precise location because it is not physically distinct from other portions of the brainstem. The sneeze center sends nerve signals back to the body through numerous nerve pathways that activate a coordinated response.

A sneeze results when the brainstem signals the VOCAL CORDS to close, allowing air pressure to build in the airway, then signals the DIAPHRAGM and various muscles in the chest, THROAT, and face to contract and the vocal cords to open. This sequence of events expels air through the nose with great force; researchers have measured sneezes leaving the nose at the equivalent of 100 miles per hour. The pressure blows mucus and irritants from the nose.

When the irritation stops, the cycle of the sneeze reflex ends. People who have a health condition such as SINUSITIS or ALLERGIC RHINITIS may sneeze so often that their noses become raw and irritated. Nasal sprays containing decongestants help reduce swelling of the nasal passages; those containing antihistamines help subdue the nose's local reaction to allergens. These approaches are often effective in reducing sneezing episodes. Increasing the moisture content of the nasal mucosa, such as by BREATHING humidified air and drinking plenty of fluids, helps relieve irritation.

Many viruses, such as those that cause COLDS and INFLUENZA, have adapted their structures to take advantage of the sneeze mechanism, using it to disperse themselves to new hosts. To reduce the spread of these infections, health experts recommend sneezing into disposable tissues and discarding them, then washing the hands thoroughly with soap and water.

Some people sneeze when they step into sunlight or look up at a sunlit sky, called photic sneezing. Doctors do not know why photic sneezing occurs, though it is an inherited trait. Some researchers speculate that sunlight (or any very bright light) stimulates brain activity near the brain's sneeze center, which sends the message to the body to sneeze. About one in four people experiences photic sneezing.

See also BAROTRAUMA; BLOWING THE NOSE; CRANIAL NERVES; HAND WASHING; NASAL VESTIBULITIS; SNEEZE/COUGH ETIQUETTE; VIRUS.

sore throat See PHARYNGITIS.

speech disorders Conditions that affect the ability of structures of the MOUTH and THROAT to form the sounds necessary for speech. Health-care providers often refer to these conditions as disorders of articulation to distinguish them from LEARNING DISORDERS that may affect speech. Learning disabilities typically involve BRAIN function, whereas speech or articulation disorders involve the mechanics of speech.

Many speech disorders arise from structural anomalies that become apparent during early childhood, such as CLEFT PALATE/CLEFT PALATE AND LIP, incorrect placement of the TEETH as they erupt, or deviations in the size and shape of the oral cavity. Functional difficulties, such as tongue control and lip placement during articulation, may also cause or contribute to speech disorders. HEARING

LOSS, neurologic conditions that affect control of the muscles of the face and throat, and brain injury are additional factors that influence the ability to speak, particularly in adults. STROKE is a leading cause of speech disability in adults.

Symptoms of speech disorders range from the obvious to the subtle and may include

- omitted sounds, in which certain consistent sounds do not appear in speech, for example, leaving the starting or ending consonants off words
- substituted sounds, in which one sound substitutes for another, such as *w* for *r* (*wabbit*)
- distorted sounds, in which extra noises such as whistling or whooshing accompany certain words or letters
- slurred, slow sounds, called dysarthria, which represent an inability to coordinate the neurologic and muscular functions necessary for speech

Speech disorders may indicate disorders of brain function; a comprehensive NEUROLOGIC EXAMINATION helps make this determination. Speech difficulties that suddenly arise suggest a physical basis, such as injury to the brain (stroke) or damage to the NERVE pathways between the brain and the face. Speech disorders may also appear as a component of learning disabilities and other developmental factors. In children, the reasons for speech disorders sometimes remain unclear, though speech therapy often can eliminate the symptoms.

The first goal of treatment is to remedy any apparent physical causes such as cleft palate or misaligned teeth. Other treatment targets strengthening the muscles of the tongue and face in conjunction with learning proper placement of the tongue and lips during speech. This is the venue of speech therapy, which provides instruction to help with forming the mouth positions and movements necessary for articulation. The speech therapist, also called speech-language pathologist, may use video and audio recordings in combination with physical findings to assess the extent and possible causes of speech disorders and to develop methods to overcome the difficulties. With appropriate treatment, most people experience improvement, and many people experience complete restoration, of speech. Children may need ongoing speech therapy as their facial features continue to grow and change.

See also APHASIA; VOICE THERAPY.

swallowing disorders Conditions that impair the functions of the muscles and nerves of the THROAT, interfering with the ability to swallow. The clinical term for this impairment is dysphagia. Swallowing disorders often exist with neuromuscular disorders such as AMYOTROPHIC LATERAL SCLEROSIS (ALS) and MUSCULAR DYSTROPHY, and as a consequence of damage to portions of the BRAIN resulting from STROKE or TRAUMATIC BRAIN INJURY (TBI). Dysphagia can affect any aspect of the swallowing process, from chewing to entry of the swallowed material into the STOMACH. Swallowing problems in young infants may indicate structural anomalies. Swallowing disorders are common among the elderly and in people of any age who have significant physical debility.

The symptoms of swallowing disorders may vary in severity and sometimes with circumstances. For example, dysphagia may manifest when the person is very tired or eats certain foods though not be apparent at other times. Symptoms may include

- SIALORRHEA (drooling)
- extended chewing because the food will not move to the back of the throat for swallowing
- difficulty initiating swallowing
- inability to swallow certain kinds of substances such as liquids
- frequent choking
- weight loss (secondary to inability to consume adequate calories)

The diagnostic path includes a careful health history and complete physical examination. Swallowing studies evaluate the coordination and control of muscles involved in moving food from the MOUTH to the stomach. A BARIUM SWALLOW X-ray, in which the person swallows a solution containing barium that coats the ESOPHAGUS, or videofluoroscopy can show irregularities in the passageway to the stomach. COMPUTED TOMOGRAPHY (CT) SCAN or

MAGNETIC RESONANCE IMAGING (MRI) can provide added visualization of the throat and upper gastrointestinal tract. Laryngoscopy allows the doctor to examine the structures of the inside of the throat. The diagnostic path may also include a NEUROLOGIC EXAMINATION to determine the presence of conditions such as PARKINSON'S DISEASE that can affect the ability to swallow.

Treatment depends on the underlying cause. Sometimes medications to relax certain muscles or reduce the flow of saliva improve the functions of chewing and swallowing. Swallowing therapy (provided by a speech-language pathologist) can teach methods to strengthen muscles and improve coordination of the steps of swallowing as well as ways to prepare food and position it in the mouth for most effective swallowing. BIOFEEDBACK is helpful for some people. Surgery may be necessary to correct esophageal strictures that narrow the passageway for food.

Most people experience improvement with treatment, though swallowing disorders resulting from degenerative conditions such as Parkinson's disease are likely to worsen as the disease progresses. In such situations, alternatives such as ENTERAL NUTRITION or PARENTERAL NUTRITION (supplemental or replacement feedings) may become necessary. Family members of those who have swallowing disorders should know how to perform the HEIMLICH MANEUVER to dislodge food that becomes aspirated into the TRACHEA.

See also ACHALASIA; CALORIE.

swimmer's ear See OTITIS.

T

toothache PAIN in a tooth or in the jaw. Toothache typically suggests DENTAL CARIES (cavities) or other dental problems. Dentists provide care when this is the case. Early intervention minimizes tooth loss, the extent of other damage such as to the gums and jaw, and the extent of treatment.

Persistent jaw pain, particularly when it extends from the shoulder into the neck and jaw, can be an early warning sign of HEART ATTACK. A physician should evaluate such pain without delay.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen and naproxen effectively relieve most tooth pain in the short term. Topical anesthetics or products containing clove oil, designated for oral use (use in the mouth), temporarily relieve pain when applied to the tooth surface or surrounding gum tissue. Good ORAL HYGIENE and adequate dietary calcium and vitamin D help maintain tooth health.

A toothache sometimes indicates health conditions such as SINUSITIS (sinus infection), OTITIS (ear infection), migraine HEADACHE, TEMPOROMANDIBULAR DISORDERS, and NEURALGIA (INFLAMMATION and irritation) affecting the nerves that supply the face. Physicians provide care for these conditions.

See also GINGIVITIS; PERIODONTAL DISEASE; TEETH.

throat The collective term for the structures at the back of the MOUTH that provide passage to the structures and organs of the trunk. The throat includes the pharynx, which carries food to the ESOPHAGUS and air to the TRACHEA, and the larynx, or voice box, which contains the VOCAL CORDS. The tonsils are at the back and top of the throat; the tongue extends to the front and top of the throat. A "sore throat" typically refers to discomfort involving any of these structures. The muscles of the throat participate in swallowing, BREATHING, and speech. The Adam's apple, a bulge in the CARTILAGE visible on the front of the throat (more visible in men than women though present in both) marks the position of the THYROID GLAND and PARATHYROID GLANDS.

COMMON CONDITIONS AFFECTING THE THROAT

ADENOID HYPERTROPHY	COUGH
CROUP	EPIGLOTTITIS
LARYNGEAL CANCER	LARYNGITIS
LARYNGOCELE	OBSTRUCTIVE SLEEP APNEA
PERITONSILLAR ABSCESS	PHARYNGITIS
POSTNASAL DRIP	SWALLOWING DISORDERS
TONSILLITIS	VELOPHARYNGEAL INSUFFICIENCY
VOCAL CORD CYST	VOCAL CORD NODULE
VOCAL CORD PARALYSIS	VOCAL CORD POLYP

For further discussion of the throat within the context of otolaryngologic structure and function please see the overview section "The Ear, Nose, Mouth, and Throat."

See also NOSE.

thrush A yeast (FUNGUS) INFECTION of the inner MOUTH. The fungus *Candida albicans* causes thrush, which appears in the mouth as reddened patches with a white discharge. Doctors may use the broader terms CANDIDIASIS or moniliasis. *C. albicans* is a common fungus present in the healthy body, kept in check by the BACTERIA that are also present. It becomes pathogenic (disease causing) only when there are disturbances to the body's natural balance that allows it to flourish.

Thrush is most common in infants between the ages of 1 month and 10 months, though it can

occur at any age. Often, and especially in infants, doctors do not know what disturbs the balance to allow thrush to develop. Known causes include treatment with ANTIBIOTIC MEDICATIONS, as antibiotics reduce the overall level of bacteria in the body. IMMUNE DISORDERS such as HIV/AIDS often prevent the body from adequately controlling its bacterial balance.

Doctors generally diagnose thrush based on appearance of the characteristic lesions (patches) in the mouth. Sometimes the doctor will gently scrape away the white surface of a LESION, which reveals the underlying reddened sore and confirms the diagnosis. Treatment is rinsing the mouth with an antifungal solution such as nystatin oral suspension. For young infants, dabbing the solution onto the lesions is sometimes more effective. Treatment continues for 48 hours after the last lesion disappears. *C. albicans* also can erupt as DIAPER RASH and vaginal infection.

See also LEUKOPLAKIA; VAGINITIS.

tinnitus The perception of a ringing, humming, roaring, or rushing sound in the EAR when there is no external auditory stimulation. Tinnitus may affect one ear or both ears. There is a growing view among otolaryngologists that tinnitus is an early indication of sensorineural HEARING LOSS, heralding damage (temporary or permanent) to the HAIR cells within the COCHLEA that translate sound waves into NERVE messages. Tinnitus is a common symptom of various vestibular disorders such as ACOUSTIC NEUROMA and MÉNIÈRE'S DISEASE. Numerous medications also can cause tinnitus, notably ANTIBIOTIC MEDICATIONS known as aminoglycosides (such as gentamicin and streptomycin) and loop diuretics (such as furosemide).

Occasionally tinnitus results from health conditions that affect the flow of BLOOD in the head, such as HYPERTENSION (high BLOOD PRESSURE) and ATHEROSCLEROSIS. These conditions may increase the turbulence of the blood, making it possible to hear the blood as it flows through the arteries. When these conditions are severe enough, the doctor can also hear the sounds by listening through a stethoscope placed at various locations on the head.

Tinnitus is common, with some experts asserting that nearly every adult will experience the symptom at some time in his or her life. Many people live with low-grade tinnitus that, though annoying when noticed, generally does not affect daily living. For some people, however, tinnitus is severe enough to interfere with concentration and even hearing to the extent of causing disability. Any health conditions that diminish the movement of sound into the ear from the external environment, such as accumulated CERUMEN or an ear INFECTION (OTITIS media or otitis externa) can intensify the tinnitus.

The diagnostic path begins with an otoscopic examination to look for obvious blockages or other physical causes. The doctor will also request a comprehensive AUDIOLOGIC ASSESSMENT to determine whether any hearing loss exists; this helps narrow the potential reasons for the tinnitus. Treatment targets the underlying cause. There are few effective treatments for idiopathic tinnitus (tinnitus that is present without an apparent cause) or for tinnitus that accompanies PRESBYCUSIS (age-related hearing loss). Many people benefit from using intentional background noise (sound masking) to mitigate the tinnitus and from learning conscious refocusing methods.

See also HEARING AID; OTOTOXICITY.

tonsillitis An INFECTION of the tonsils (lymph structures at the back of the THROAT). Tonsillitis is common and often recurrent in children. Conventional wisdom holds that the tonsils (and the nearby ADENOIDS) serve to produce antibodies to help the body protect itself against invading pathogens (disease-causing agents such as viruses and BACTERIA). However, in the modern environment there is an overwhelming abundance of pathogenic agents, which many health experts believe accounts for the prevalence of tonsillitis. Some researchers believe that the tonsils are becoming, or have become, vestigial structures akin to the appendix.

The characteristic symptoms of tonsillitis are

- PAIN and swelling at the back of the throat
- difficulty swallowing
- FEVER
- HEADACHE

The tonsils may appear enlarged and reddened, and may ooze pus or be covered in small white

dots. The infectious agent may be viral or bacterial; the doctor is likely to swab the throat to perform a rapid strep test to check for streptococci bacteria. Streptococci tend to migrate to other parts of the body such as the HEART valves, making any strep infection potentially dangerous. A throat culture can determine the presence of other pathogenic bacteria. Bacterial tonsillitis, including STREP THROAT requires treatment with ANTIBIOTIC MEDICATIONS. Viral tonsillitis generally runs its course within two weeks. In either case, ANALGESIC MEDICATIONS such as acetaminophen or ibuprofen can provide pain and fever relief.

Children should not receive aspirin for pain or FEVER because of the potential for REYE'S SYNDROME, a rare but serious complication.

The otolaryngologist may recommend tonsillectomy (an OPERATION to remove the tonsils) when recurrent tonsillitis causes the tonsils to remain enlarged to the extent that they interfere with BREATHING. Indications of this include loud snoring when sleeping and mouth breathing when awake, particularly in children. Enlarged tonsils can cause OBSTRUCTIVE SLEEP APNEA, in which there are episodes during sleep when the person does not breathe. In the normal course of development, the tonsils atrophy (shrink) as ADOLESCENCE approaches, and by early adulthood tonsillitis is uncommon. For this reason many doctors prefer to manage tonsillitis medically rather than surgically unless ANTIBIOTIC RESISTANCE develops.

See also EPIGLOTTITIS; LARYNGITIS; OTITIS; PHARYNGITIS; PERITONSILLAR ABSCESS; SINUSITIS; VIRUS.

tympanic membrane A thin piece of tissue that stretches across the base of the auditory canal (EAR canal). The tympanic membrane, commonly called the eardrum, vibrates in response to sound waves that reach it by traveling from the outer ear through the auditory canal. The vibrations amplify the sound waves, which activate the auditory ossicles, tiny bones in the middle ear, to set in motion the cascade of events that results in NERVE signals traveling to the BRAIN.

The tympanic membrane is vulnerable to perforation, commonly called RUPTURED EARDRUM. Perforation may occur as a result of injury, such as penetration of an object or from a sharp blow to the outer ear, or spontaneously. Fluid accumulation in the middle ear behind the tympanic membrane, usually the consequence of INFECTION, is the most common cause of spontaneous perforation. Spontaneous perforation generally heals without intervention. Traumatic perforation may require surgical repair (TYMPANOPLASTY).

In addition to amplifying and transferring sound waves, the tympanic membrane protects the middle and inner ear from bacteria and debris. A perforated eardrum exposes the delicate structures behind it to possible infection and other damage. Repeated spontaneous perforation due to chronic OTITIS media (middle ear infection) can permanently scar the tympanic membrane, restricting its ability to vibrate. The otolaryngologist may insert a small tube through the tympanic membrane to allow collected fluid to drain (MYRINGOTOMY) as a preventive measure in children who have chronic ear infections.

See also CLEANING THE EAR; FOREIGN OBJECTS IN THE EAR OR NOSE; HEARING LOSS; MYRINGITIS.

tympanoplasty Surgical reconstruction of the TYMPANIC MEMBRANE (eardrum). Damage to the tympanic membrane can occur as a result of scarring due to repeated OTITIS media (middle EAR INFECTION), traumatic injury, and acquired defects such as might remain following removal of a CHOLESTEATOMA (pocketlike growth). The otolaryngologist cuts out a small piece of FASCIA (thin connective tissue that covers muscle) from the temporal MUSCLE at the point of incision behind the ear when the OPERATION begins; this becomes the new tympanic membrane. Restoration of hearing varies and may depend on factors not related to the tympanoplasty. Infection, which may be present in the middle ear at the time of the surgery, can cause the new tympanic membrane to fail. About 80 percent of adults who undergo tympanoplasty experience improvement in hearing and reduced otitis.

See also MYRINGOTOMY; OTOPLASTY; RHINOPLASTY; SURGERY BENEFIT AND RISK ASSESSMENT.

V

velopharyngeal insufficiency Inadequate closure the velopharyngeal sphincter, a MUSCLE at the back of the soft palate, that directs air flow to the NOSE or to the MOUTH. Velopharyngeal insufficiency often accompanies CLEFT PALATE/CLEFT PALATE AND LIP anomalies and interferes with both speech and swallowing. It also can occur as a complication of tonsillectomy and adenoidectomy, operations to remove the tonsils and ADENOIDS, respectively, and of neurologic damage, such as from STROKE, that restricts neuromuscular function of the pharynx. The hallmark symptoms of velopharyngeal insufficiency are nasal speech and regurgitation food into the back of the nose with swallowing. Sometimes the person has chronic or recurrent SINUSITIS resulting from food particles becoming trapped in the sinuses. The doctor may be able to feel a previously undiagnosed cleft in the hard palate beneath an intact soft palate. ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN can confirm the diagnosis.

Treatment for velopharyngeal insufficiency when the cause is a structural anomaly begins with surgery to restore sphincter function to the extent possible. Operations may include repair of a cleft palate or reconstructive surgery to extend the soft palate (pharyngoplasty) to make the velopharyngeal opening smaller. Most people subsequently need speech therapy to retrain oral-facial structures to form the sounds the velopharyngeal insufficiency kept them from properly making. These therapeutic interventions typically restore complete function, though may not be appropriate or successful when the cause of the velopharyngeal insufficiency is neurologic damage or a neuromuscular disorder.

See also OPERATION; SPEECH DISORDERS; SURGERY BENEFIT AND RISK ASSESSMENT; SWALLOWING DISORDERS.

vertigo The perception of movement, usually spinning, when none is taking place. Vertigo represents the body's inability to accurately interpret its position and movement within its environment. People with vertigo feel either that they are moving or the setting around them is moving. Vertigo occurs when the balance mechanisms of the vestibular system, including the NERVE pathways to the BRAIN, malfunction. The disturbance can range from mild and brief to extended and debilitating. Vertigo is a symptom of numerous health conditions that can be vestibular (affecting the structures of the inner EAR) or neurologic (affecting the brain or nerves). Situations that overstimulate the vestibular system, such as spinning rapidly in circles (as in carnival rides) or experiencing gravitational force (as in taking off in a jet or a space shuttle), also often generate temporary vertigo.

Causes of Vertigo

Vertigo develops when the brain receives conflicting or incomplete information from the vestibular system about the body's orientation in its environment. This can occur because injury or disease damages the structures of the vestibular system or the parts of the NERVOUS SYSTEM that convey balance and movement information to the brain. Brain injury, such as from trauma or STROKE, that affects parts of the brainstem involved in movement also can result in vertigo.

Most commonly vertigo reflects dysfunction of the vestibular system and the structures of the inner ear. The semicircular canals, three fluid-filled loops, detect rotational movements. The saccule and the utricle, also fluid-filled chambers, detect linear (horizontal and vertical) movements.

The nerve cells in these structures send a continuous stream of signals to the movement centers of the brain, which in turn direct the muscles to respond in ways that keep the body upright and stable. This flow of communication takes place immeasurably fast and without conscious awareness, as long as all components of the system are functioning properly.

Situational disruptions of vestibular functions (such as a carnival ride creates) resolve spontaneously when the stimulatory overload stops and the body returns to normal functions, though residual sensations of NAUSEA or queasiness may remain. Pathologic disruptions—changes brought about by damage or disease—often result in persistent balance disturbances, the key symptom of which is vertigo.

Relieving Vertigo

Situational vertigo, such as from spinning in circles, resolves itself when the environmental stimulation stops. When vertigo is pathologic, certain ANTIHISTAMINE MEDICATIONS, commonly marketed for relief of motion sickness, often provide relief. Researchers do not know the mechanisms through which antihistamines intercede with vestibular functions. Most antihistamines that can relieve vertigo also cause substantial drowsiness, making them unsuitable in situations that require alertness and concentration.

Maintaining the focus of the eyes on the direction of movement can help stabilize the vestibular system. This method provides additional information to the brain via sight about the body's position and movement. It also is a diagnostic device in helping distinguish the nature of the dysfunction: vestibular or neurologic. Many people obtain relief from ACUPUNCTURE and acupressure. Pressure bands are available that activate the acupuncture points on the inner wrists; rubbing the earlobes activates the acupuncture points there.

Surgical interventions may become necessary to treat severe, unremitting vertigo that becomes disabling. These are procedures of final resort, as they create permanent disruptions in the vestibular system such as severing the vestibular nerve or removing the labyrinthine structures of the inner ear. Because the function of hearing also uses these structures, surgical interventions are typically viable options only when there is also profound and irreversible HEARING LOSS.

Preventing Vertigo

Situational vertigo is preventable by avoiding the circumstances that cause it. Pathologic vertigo results from underlying disease processes that often are not possible to mitigate. Methods such as focusing the eyes in the direction of movement can sometimes minimize a vertigo episode. Some vertigo is positional, so avoiding the positions prevents the vertigo. Quick movements of the head, particularly upward, are known to bring on vertigo in many conditions in which vertigo occurs (such as Ménière's disease).

Space flight is providing an ideal opportunity for researchers to study the mechanisms of balance and vertigo, as nearly all astronauts experience vertigo under the extreme gravitational and centrifugal forces to which leaving and reentering the earth's gravitational field subjects them as well as the absence of gravity during space flight. The normally functioning vestibular system uses gravity as its point of reference for determining the body's position and movement. Researchers hope that gaining understanding of how the body adapts to the absence of gravity will shed light on how the vestibular system functions as well as dysfunctions, leading to new preventions and treatments for vertigo and the conditions for which it is a symptom.

See also ACOUSTIC NEUROMA; BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV); LABYRINTHITIS.

vestibular neuronitis A dysfunction of the vestibular system that causes sudden and severe VERTIGO (sensation of spinning) with accompanying NAUSEA, VOMITING, and balance disturbances. The prevailing view is that viral infections cause vestibular neuronitis. Because hearing remains unaffected, doctors believe the INFECTION inflames the vestibular NERVE, the branch of the eighth cranial nerve (vestibulocochlear nerve) leading from the vestibular structures to the BRAIN. INFLAMMATION causes the vestibular nerve to transmit confused and erroneous signals to the brain. The brain responds to the incoming signals as though

they were legitimate, instructing the body to react to movement that is not occurring or failing to direct reaction when there is movement. This confusion results in vertigo and a sense of spatial disorientation. Vestibular neuronitis most commonly occurs in adults between the ages of 40 and 60.

Symptoms and Diagnostic Path

The distinguishing symptoms of vestibular neuronitis are severe vertigo and one-sided balance disturbances without TINNITUS or HEARING LOSS. Any hearing-related symptoms suggest a different diagnosis. The vertigo causes nausea and often vomiting. Attempts to move, or to move the head, result in repeated vertigo. The symptoms often are debilitating, with the person falling toward the affected side when attempting to walk and sometimes when attempting to sit upright. Symptoms appear abruptly though often follow a cold or occur among groups of people who are in close contact. An initial episode of symptoms can last 7 to 10 days.

The diagnostic path is fairly straightforward; any pattern of vestibular disturbance that includes additional symptoms is likely to have a different cause. Confirming diagnostic signs the doctor looks for include

- horizontal NYSTAGMUS (rapid movements of the EYE with certain positions or movements)
- diminished or absent response to caloric testing (alternating warm and cool water infused into the auditory canal)

Imaging procedures are not likely to offer diagnostic information unless the doctor is uncertain of the diagnosis, in which case MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN can rule out other conditions such as ACOUSTIC NEUROMA.

Treatment Options and Outlook

The VIRUS causing the vestibular neuronitis must run its course, which typically takes 10 to 14 days. During this time, certain ANTIHISTAMINE MEDICATIONS used to treat motion sickness can provide relief from the vertigo and associated nausea. These antihistamines include the prescription medications hydroxyzine (Atarax, Vistaril) and promethazine (Phenergan) and the over-the-counter products dimenhydrinate (Dramamine), meclizine (Antivert, Bonine) and diphenhydramine (Benadryl). The two prescription medications diazepam (Valium) and clonazepam (Klonopin) appear to act on the vestibular system directly to subdue the vertigo, though cause more sedation than antihistamines and can be addictive when used for an extended period of time. ACUPUNCTURE gives some people relief. Most people recover completely and are free from residual consequences in three to four weeks. A small percentage experiences recurrent episodes over the following months to years, though the severity of symptoms diminishes with each episode.

Risk Factors and Preventive Measures

Because doctors do not know for certain what causes vestibular neuronitis, they cannot identify risk factors or preventive measures. Prompt diagnosis and treatment help relieve symptoms more quickly but do not appear to alter the course of the inflammation or affect the likelihood of RECURRENCE.

See also CRANIAL NERVES; BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV); LABYRINTHITIS; MÉNIÈRE'S DISEASE.

vocal cord cyst A saclike growth on the vocal cord that usually develops as a result of persistent irritation such as from smoking or GASTROESOPHAGEAL REFLUX DISORDER (GERD), which may flush the VOCAL CORDS with gastric juices when an individual is lying down and especially when he or she is sleeping. A vocal cord cyst often contains fluid though can contain solid tissue. A cyst can develop deep within the vocal folds, causing significant changes or difficulties with the voice. The primary symptom of vocal cord cyst is hoarseness. Though vocal cord cysts are noncancerous, otolaryngologists generally operate to remove them because they tend to enlarge. Endoscopic surgery allows the otolaryngologist to remove most vocal cord cysts through the THROAT. Recovery from the surgery takes two to four weeks; most people benefit from follow-up VOICE THERAPY to teach methods for preserving vocal cord integrity and voice quality.

See also OPERATION; SMOKING AND HEALTH; VOCAL CORD NODULE; VOCAL CORD POLYP.

vocal cord nodule A noncancerous, fibrous growth on the vocal cord, usually the result of overusing the voice through repeated shouting, singing, or public speaking. Vocal cord nodules typically develop in book-matched pairs on the folds of the VOCAL CORDS at points where the cords vibrate in contact with each other. Nodules arise from the epithelium, or surface layer of tissue, that covers the vocal cords (unlike vocal cord polyps, which arise from the mucous membrane that forms the vocal cords). Vocal cord nodules have the appearance of calluses and cause the voice to take on a "breathy" quality, though some people also experience hoarseness. The otolaryngologist can remove vocal cord nodules through the THROAT using endoscopic surgery. The surgical wound takes about six weeks to heal, after which VOICE THERAPY helps the person learn methods to protect the vocal cords and voice. Because vocal cord nodules develop through overuse, they are likely to recur with continued extensive speaking or singing.

See also VOCAL CORD CYST; VOCAL CORD POLYP.

vocal cord paralysis The inability of the vocal cord, a membranous flap of tissue in the larynx, to open or close properly with the passage of air. PARALYSIS may affect one vocal cord or both VOCAL CORDS. Paralysis that affects both vocal cords is rare and often affects BREATHING, as air cannot move freely through the THROAT. Symptoms include hoarseness, a "breathy" quality to the voice, diminished vocal volume, and occasionally throat PAIN. Vocal cord paralysis often develops without an identifiable cause, though also results from injury to the throat or nerves that supply the throat, BRAIN injury (such as trauma or from STROKE), and neurologic conditions such as MULTIPLE SCLEROSIS and PARKINSON'S DISEASE. People who use their voices extensively, such as singers and teachers, are especially prone to vocal cord paralysis.

The diagnostic path typically includes laryngoscopy to examine the larynx and vocal cords. Because vocal cord paralysis often goes away on its own, doctors often take a watchful waiting approach in combination with VOICE THERAPY to improve voice function and quality. If the paralysis continues, the otolaryngologist can inject a bulking agent such as collagen into the paralyzed cord. This closes the gap between the cords and encourages both sets of cords to vibrate equally. These measures improve, and often restore, vocal cord function.

See also SPEECH DISORDERS; SWALLOWING DISORDERS; VOCAL CORD CYST; VOCAL CORD NODULE; VOCAL CORD POLYP.

vocal cord polyp A fleshy growth on the vocal cord. Vocal cord polyps occur singly, rather than paired as do vocal cord nodules, though more than one polyp may be present. A polyp arises from the mucous membrane that forms the VOCAL CORDS; it grows out from the vocal cord on a stem-like appendage, which allows the polyp to move freely as the vocal cord vibrates. The location and size of the polyp determine the ways that it interferes with speech and hence its symptoms, which can include a "breathy" quality to the voice, hoarseness, difficulty "starting" the voice, and sometimes loss of the voice.

Polyps develop as a result of irritation such as from smoking, chronic POSTNASAL DRIP, environmental pollutants, and allergic PHARYNGITIS. Because polyps in other locations of the body, such as the intestines and the SINUSES, occasionally become cancerous, otolaryngologists recommend prompt surgical removal. Most people fully recover within four to six weeks. VOICE THERAPY can teach methods to preserve and protect the voice. Continued exposure to the causative irritants, such as cigarette smoke, is likely to result in recurrent polyps.

See also OCCUPATIONAL HEALTH AND SAFETY; OPERATION; SMOKING AND HEALTH; VOCAL CORD CYST; VOCAL CORD NODULE.

vocal cords A paired fold of thick, fibrous tissue in the back of the larynx that vibrate with the passage of air to produce sounds. The vocal cords run lengthwise in the larynx. Muscles that attach the vocal cords to the larynx contract and relax to change the tautness of the vocal cords, producing variations in sound tone and volume. The vocal cords relax during BREATHING to allow free passage of air through the larynx. The "talk test" for AEROBIC EXERCISE is an indirect measure of the volume of air flowing through the THROAT: being unable to speak during exercise means air flow is high enough that the vocal cords cannot contract.

Singing and extended talking can greatly strain the vocal cords, resulting in inflammation (LARYNGITIS) that causes the voice to sound scratchy or hoarse. Environmental irritants such as pollen or smoke can also cause laryngitis. Cigarette smoking is particularly stressful for the vocal cords, causing extended irritation that may result in chronic hoarseness and growths such as a VOCAL CORD CYST or VOCAL CORD POLYP. Cancerous tumors related to smoking can develop on the vocal cords. Loss of the vocal cords, such as due to LARYNGECTOMY (surgical removal of the larynx) for laryngeal CANCER, results in loss of the voice.

For further discussion of the vocal cords within the context of otolaryngologic structure and function please see the overview section "The Ear, Nose, Mouth, and Throat."

See also CONDITIONING; ESOPHAGEAL SPEECH; SMOKING AND HEALTH; VOICE THERAPY.

voice therapy Methods and techniques for improving the ability of the larynx (voice box) to produce speech. Voice therapy focuses on the mechanical aspects of vocal cord function, MUSCLE control and coordination, and breath control. Voice therapy typically follows operations on the VOCAL CORDS and larynx to restore voice volume and quality. Professionals who use their voices, such as singers and lecturers, may find voice therapy beneficial in overcoming the deleterious effects of overusing the voice. A voice therapist also may work with a person who has had a LARYNGECTOMY (surgical removal of the larynx) to improve the quality of alternate articulation methods such as ESOPHAGEAL SPEECH or ELECTROLARYNX speech.

The techniques of voice therapy vary according to the diagnosed speech disorder or clinical situation, the person's speaking needs, and the desired outcome. Voice therapy may incorporate resting the voice completely, which allows only 15 minutes of total voice use in a 24-hour period of time. Other techniques focus on using the breath to generate voice volume and quality, and learning to adjust the pitch of the voice rather than only volume to add emphasis to speech.

See also OPERATION; VOCAL CORD PARALYSIS.

THE EYES

The eyes conduct the function of vision. Practitioners who provide care for the eyes and vision may be ophthalmologists (medical doctors who specialize in ophthalmology, providing medical and surgical treatment for diseases of the EYE) or optometrists (doctors of optometry who specialize in diagnosing and correcting REFRACTIVE ERRORS of vision). This section, "The Eyes," presents a discussion of the structures of the eye and how they function to provide the sense of sight, an overview of VISION HEALTH and disorders, and entries about the health conditions that can affect the eyes and vision.

Structures of the Eye

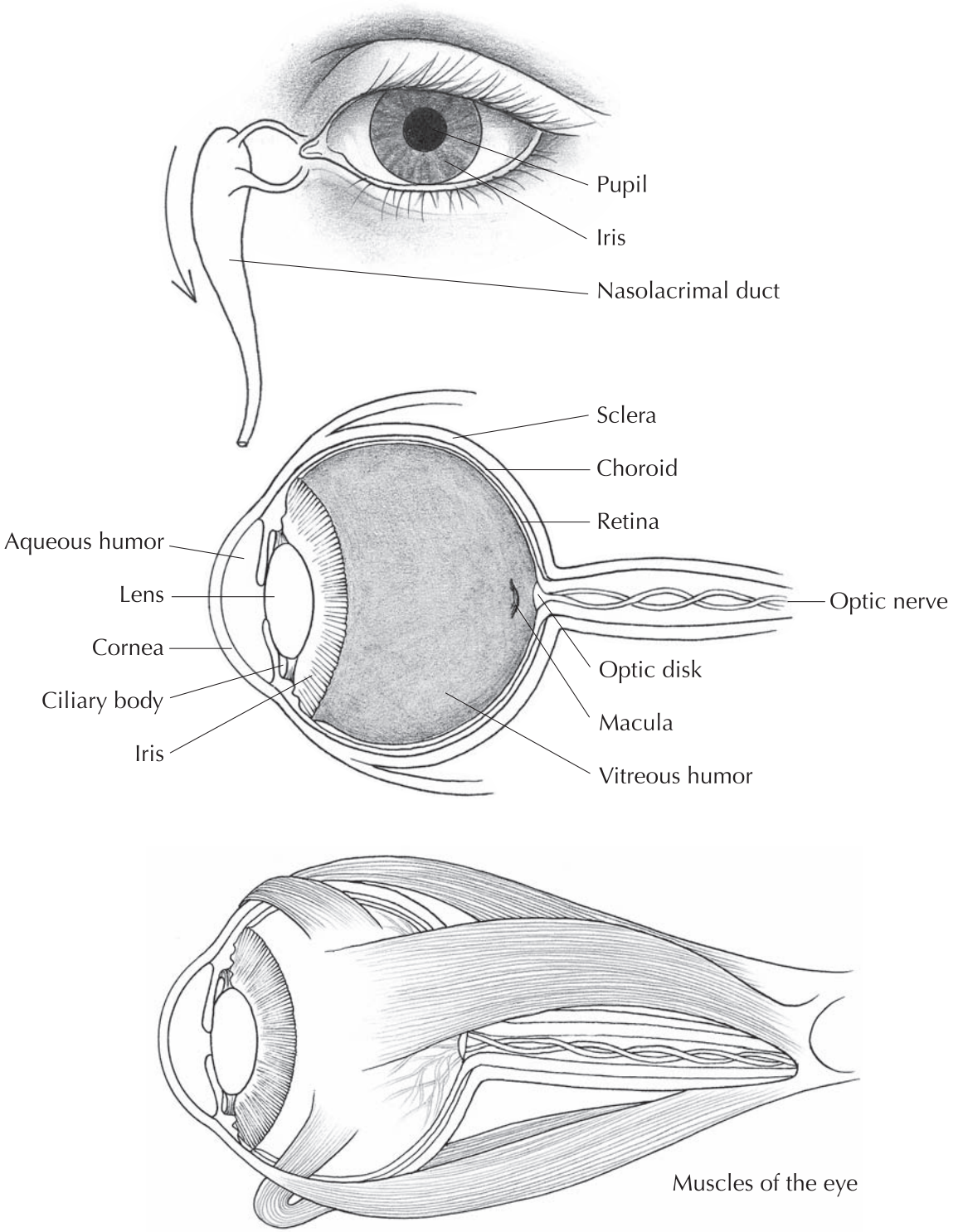
- EYELIDS
- LACRIMAL (TEAR) GLANDS
- CONJUNCTIVA
- SCLERA
- CORNEA
- CHOROID
- RETINA
  - RODS
  - CONES
  - MACULA
  - OPTIC DISK
- IRIS
- PUPIL
- ANTERIOR CHAMBER
- AQUEOUS HUMOR
- LENS
- POSTERIOR CHAMBER
- CILIARY BODY
  - CILIARY PROCESSES
  - CILIARY MUSCLES
- VITREOUS HUMOR
- OPTIC NERVE

Functions of the Eye

Ancient philosophers viewed the eyes as the windows to the soul, based on the belief that the PINEAL GLAND, located deep within the BRAIN, held the soul. Their rudimentary understanding of anatomy and physiology led them to conclude that the optic nerves connected the pineal gland and the soul directly to the outside world through the eyes. Though modern knowledge of the body's structure and function clarifies that no such physical pathway exists, ancient scientists were not entirely off track. The pineal gland does appear to receive direct information from the external environment, which influences its production of MELATONIN, a HORMONE related to the body's circadian cycles (cycles of wakefulness and sleep). Researchers do not fully understand the mechanisms of this, and it is possible the OPTIC NERVE plays some role. However, the primary function of the optic NERVE is to provide a direct conduit from the EYE to the brain through which the brain receives about two thirds of the information it processes about the environment outside the body.

The eye resides within the protective enclosure of the orbit, a socket of BONE in the skull. Thin pads of fat cover the orbital bones to cushion the eye. A small opening in the back of the orbit allows passage of the optic nerve and the blood vessels that supply the eye. The eyelids, upper and lower, blink—automatically open and close—15 to 20 times a minute to rinse the eye with tears. Reduced blink rate is a characteristic of neurologic disorders such as PARKINSON'S DISEASE; increased blink rate occurs with eye irritation such as CONJUNCTIVITIS and diseases such as MENINGITIS. The tears then drain from the lacrimal sac at the inner corner of the eye into the upper NOSE. The eyelids also close to protect the eye from hazards such as foreign objects and very bright light, and to cover the eye during sleep to keep it moist. The eyelashes, extending from the eyelids, also help keep foreign objects from striking the eye and the eyebrows channel sweat around the eyes.

Six muscles attach the eye to the orbit, functioning in pairs as well as in coordination with one another to move the eye. These muscles integrate into the sclera, the fibrous outer layer of the eye, and extend to the back of the orbit where they anchor to the bone. When one MUSCLE in a pair contracts, the other relaxes. Typically both eyes move in tandem, which allows the eyes to simultaneously focus on the same object. This


Pupil
Iris
Nasolacrimal duct
Sclera
Choroid
Retina
Aqueous humor
Lens
Cornea
Ciliary body
Iris
Optic nerve
Optic disk
Macula
Vitreous humor
Muscles of the eye

provides depth perception and accommodates each eye's "blind spot." Some people have the ability to intentionally move their eyes independent of each other, though unintentional disparate movement generally indicates a pathologic condition. Discordant movement may characterize neurologic disorders such as progressive supranuclear palsy (PSP) and TRAUMATIC BRAIN INJURY (TBI). Abnormal eye movements also accompany vestibular disorders (disturbances of the balance mechanisms of the inner EAR).

MUSCLES THAT MOVE THE EYE

- ***Superior oblique*** and ***inferior oblique*** rotate the eye primarily in a circular motion.
- ***Superior rectus*** and ***inferior rectus*** move the eye primarily up and down.
- ***Lateral rectus*** and ***medial rectus*** move the eye primarily side to side.

How the eye "sees" The sclera gives the eye its shape and rigidity. The front part of the sclera forms the "white" of the eye, the coloration coming from the white pigmentation of the fiber cells. In its center, the sclera becomes transparent, forming the CORNEA. The middle layer of the eye's wall is the choroid, a thin, dark membrane rich in BLOOD vessels. The choroid loosely attaches to and nourishes the sclera and the eye's innermost layer, the RETINA, where sight becomes vision.

Specialized cells infuse the retina, which lines the back of the inner eye. These cells, rods and cones, convert lightwaves into electrical impulses. Rods are the most plentiful, numbering about 120 million on each retina, and detect light in perceptions of shades of gray. Cones detect color and detail; there are about 6 million of them on each retina. Cones are sensitive to red, green, or blue. Rods and cones contain photosensitive chemicals that react to different wavelengths of light. The reactions alter the electrical charges of the rods and cones, creating nerve signals. Each minute of wakefulness thousands of these impulses traverse the optic nerves, carrying messages the brain then interprets and assembles as visual images.

The optic nerve, which contains more than a million nerve fibers, carries these signals to the brain. The pigmented cells of the retina are rich in melanin, the same chemical that causes the SKIN to darken in response to sun exposure. In the retina, these cells form a "blackout screen" that eliminates reflection, allowing lightwaves to reach and activate the rods and cones without interference. The macula, a small circular area in the center of the retina, contains the most dense distribution of cones and handles fine detail vision. The "blind spot," the point at which the optic nerve enters the retina, is the optic disk; it contains no rods or cones. RETINITIS PIGMENTOSA (hereditary degeneration of the retina) and RETINAL DETACHMENT (separation of the retina from the choroid) are among the conditions that can affect the retina, resulting in impaired vision and blindness.

The physics of vision Lightwaves pass through the cornea and the LENS to enter the eye through the pupil, the opening in the circular muscle that rings the lens, the iris. The iris is the colored part of the eye; the pupil in its center appears black because it reveals the dark interior of the eye. The iris dilates (increases the size of) the pupil to allow more light to enter the eye and constricts (decreases the size of) the pupil to reduce the light that enters the eye. The cornea and the lens each refract, or bend, the entering lightwaves. The ciliary muscles contract and relax to move the lens, which thickens or flattens, respectively, to improve focus. After about age 40 the lens gradually loses its FLEXIBILITY, accounting for age-related difficulty with near vision (PRESBYOPIA).

Refracted light forms a final focal point that, in the healthy eye, aligns in a pattern on the retina at the back of the eye. The mechanics of this refractory process are such that the image resulting on the retina is upside down. When interpreting and assembling nerve signals from the eye, the brain automatically reverses the image to perceive it right-side up. Refractive ASTIGMATISM, HYPEROPIA, and MYOPIA when the final focal point falls short of or extends beyond the retina, resulting in images that are out of focus or distorted.

Helping keep the lightwaves from fragmenting during refraction are two chambers of fluid, the aqueous humor, which fills the space between the cornea and the lens (the anterior chamber), and the vitreous humor, which fills the interior of the eye. The ciliary processes, specialized folds of the eye's choroid layer that extend into the posterior chamber at the corners of the lens behind the iris,

produce aqueous humor. This watery fluid is about the consistency of saliva and serves also to lubricate and nourish the cornea. Aqueous humor circulates through the anterior chamber between the cornea and the lens, then drains from the eye via the drainage angle, a channel between the iris and the cornea. Dysfunction of the drainage angle is a hallmark characteristic of GLAUCOMA.

Vitreous humor forms when the eye completes its development during the final trimester of gestation. A substance similar to water in chemical composition and to gelatin in consistency, vitreous humor maintains the eye's shape and helps keep the retina smooth and even against the back of the eye. The volume of vitreous humor increases as the eye grows though otherwise remains constant (unlike the aqueous humor, which the eye continuously produces). Around age 40 years the vitreous humor begins to liquefy as a normal process of aging, causing VITREOUS DETACHMENT, which usually has little effect on vision though can produce FLOATERS (fragments of tissue that become suspended in the vitreous humor).

VISION IMPAIRMENT

- ***Refractive errors*** occur when the focal point of light-waves entering the eye fails to align properly on the RETINA (ASTIGMATISM, nearsightedness, farsightedness).
- ***Functional limitations*** result when corrected vision remains insufficient to allow participation in activities or occupations that require sight.
- ***Legal blindness*** exists when corrective measures cannot restore VISUAL ACUITY to 20/200 or VISUAL FIELD to greater than 20 degrees.

Health and Disorders of the Eyes

More than 150 million Americans have a VISION IMPAIRMENT that requires CORRECTIVE LENSES (eyeglasses or contact lenses)—30 percent of men and 40 percent of women. About 12 million Americans have uncorrectable vision impairments that result in functional limitations; 10 percent of them meet the criteria for legal blindness. Among those who have uncorrectable vision impairments, 50 percent are age 65 or older. Though the eyes arise directly from the evolving brain very early in fetal development, their formation becomes complete during the final 12 weeks of PREGNANCY. Infants born before 32 weeks of gestation are at risk for RETINOPATHY of prematurity, a leading cause among children of vision impairments ranging from STRABISMUS (inability to focus both eyes on the same object) to legal blindness.

Traditions in Medical History

As refractive errors are very common, practitioners throughout history have tried various and sometimes hazardous methods for improving or restoring vision. The earliest documentation of corrective lenses for this purpose dates to 16th China. European traders who traveled to China noted the elderly holding quartz crystal lenses to see objects close to them. Eyeglasses set in frames and worn on the face began to appear in Europe in the 17th and 18th centuries. By the late 19th century inventors were experimenting with glass lenses placed directly on the eye. These attempts produced large, heavy, and ultimately unfeasible lenses that covered the entire surface of the eye. The contact lens finally became a reality in the 1950s with the advent of high-tech plastics that were lightweight, optically clear, and inert (did not react with body fluids). Subsequent advances over the next 30 years brought about lenses made of surgical plastics that allow oxygen to reach the cornea, much improving comfort and safety. By the 1990s, daily wear disposable contact lenses became the standard of contact lens correction.

CATARACT, the clouding and discoloration of the eye's lens that develops with aging, has for centuries been the leading cause of blindness in adults. It also is one of the earliest documented vision problems for which practitioners used surgical treatments to remedy, perhaps because the cause of the problem, the cloudiness, was so apparent. CATARACT EXTRACTION AND LENS REPLACEMENT has become so commonplace in contemporary ophthalmology that the procedure is no less an expectation for restoring vision than are eyeglasses for correcting refractive errors. In about 20 minutes, the ophthalmologist removes the clouded lens and replaces it with a synthetic one. Ancient physicians, lacking the benefits of the anesthetics that make the surgery painless for today's patients, became skilled at "couching" a cataract in only seconds. The procedure required the doctor to distract the patient long enough to puncture the cornea and push the lens out of the

line of vision. The lens remained within the eye as though resting, hence the term "couching." The result was less than perfect because the person lost the refractive ability of the lens, but the procedure restored enough vision to allow one to function in daily life. In the 1950s ophthalmologists began removing the cataract from the eye, but not until the 1970s did technology and technique converge in procedures that incorporated a replacement lens.

Breakthrough Research and Treatment Advances

The evolution of knowledge and advances in laser technology are converging to present treatment options that were science fiction a decade ago. New procedures are greatly expanding the potential for permanent correction of disorders and defects of the eye, including refractive disorders, that reduces and may eventually even eliminate the need for corrective lenses. Refined laser techniques such as LASIK allow ophthalmologists to reshape the cornea in precise, microscopic increments. Implantable rings inserted around the edge of the cornea can help flatten and reshape it to alter its refractive ability. Permanent contact lenses attached over the lens can have similar effect. Implantable replacement lenses are expanding beyond their initial application in cataract extraction and replacement to offer nearly ideal vision for people with severe astigmatism or myopia (nearsightedness).

Cataract extraction and lens replacement now routinely restores sight for more than 90 percent of people who otherwise would lose vision to cataracts. Other surgical procedures offer hope for altering the course of glaucoma. New treatments may stem the loss of vision due to AGE-RELATED MACULAR DEGENERATION (ARMD). These conditions are the leading causes of vision impairments that lead to functional limitations or legal blindness among adults. And research continues to explore a "bionic" PROSTHETIC EYE that can convert lightwaves to nerve impulses and transmit them to the brain. Such a prosthesis would function similarly to the COCHLEAR IMPLANT used to restore some types of neurosensory HEARING LOSS. Because many of the conditions that result in vision impairment are not preventable, technological innovations such as these appear to be the future of ophthalmologic treatment.

A

age-related macular degeneration (ARMD) A progressive condition that results in the gradual deterioration of the macula, the portion of the RETINA that provides the ability to see fine detail, and loss of vision from the center of the field of vision. ARMD is the leading cause of VISION IMPAIRMENT, resulting in functional limitations and legal blindness in people over the age of 50. ARMD develops when the retina's BLOOD supply diminishes. The macula's high concentration of cones, the cells responsible for color and fine detail vision, makes it especially vulnerable to damage and its cells begin to die. The death of the cells result in diminished vision. ARMD may affect one eye at first, though nearly always affects both eyes as it progresses.

There are two forms of ARMD, atrophic (commonly known as dry) and neovascular (commonly known as wet). All ARMD begins as the atrophic form, in which the nourishing outer layer of the retina withers, or atrophies. Approximately 90 percent of ARMD remains in this form and progresses slowly. In the remaining 10 percent, new blood vessels begin to grow erratically within the choroid, the blood-rich membrane that nourishes the retina. These blood vessels are thin and fragile, and bleed easily. The resulting hemorrhages cause the retina to swell, distorting the macula and accelerating the loss of cells.

Symptoms and Diagnostic Path

ARMD begins insidiously and people tend to attribute early symptoms to the normal changes of aging. Early symptoms include

- blurring of words when reading
- "missing pieces" in the field of vision, such as parts of words or gaps in the appearance of lines or objects
- the need for increased light to perform tasks that require close vision
- faded colors
- tendency to look slightly to the side of objects to see them clearly
- distorted or wavy lines on linear objects such as signs, doorways, and railings (suggests wet ARMD)

As the macular degeneration progresses, a blind spot in the center of vision becomes apparent and enlarges. Wet ARMD progresses far more rapidly than dry ARMD. A simple screening test called the AMSLER GRID can show the gaps in vision that occur with either form of ARMD. The ophthalmologist uses further procedures, such as OPHTHALMOSCOPY and SLIT LAMP EXAMINATION, to visualize the retina and macula and determine which form of ARMD is present and how extensive the damage. The ophthalmologist looks for signs of exudation (swelling of the tissue that oozes fluid) that suggests wet ARMD, and for drusen (spots of depigmentation on the macula that signal the loss of retinal cells). For wet ARMD, the ophthalmologist may perform a diagnostic procedure called fluorescein angiography, in which the ophthalmologist injects fluorescein dye into a VEIN and then takes photographs of the retina as the dye flows through its blood vessels.

Treatment Options

Treatment options for ARMD are limited, and at this time there really are no treatments for dry

ARMD. Some research studies demonstrate the rate of degeneration slows with increased consumption of the antioxidants lutein and zeaxanthin, and vitamins A, C, and E. For wet ARMD the laser treatments photocoagulation and photodynamic therapy are sometimes effective in sealing bleeding blood vessels and thwarting their growth, though they cannot permanently halt the neovascularization or restore vision already lost. Photocoagulation uses a hot laser to cauterize the blood vessels but also destroys cells in the vicinity of the targeted blood vessels. With photodynamic therapy, the ophthalmologist injects a photosensitive DRUG into the person's veins, then uses a cool laser to target blood vessels in the retina when the drug reaches them. The light of the laser is not intense enough to burn the tissue though activates the drug, which then destroys the blood vessels.

Outlook and Lifestyle Modifications

For most people who have ARMD vision declines slowly and may affect only one eye for a long time before affecting the other eye as well. Because the loss affects the center of the field of vision, vision loss is not complete though affects activities that require detailed focus, such as reading and driving, and typically reaches the level of legal blindness. Numerous community and health-care resources can assist with adaptive methods to accommodate diminishing vision. Even with wet ARMD, which progresses more rapidly and more severely than dry ARMD, some vision remains.

Causes and Preventive Measures

Researchers do not know what causes ARMD, though it appears to have a hereditary component in that it runs in families. There are few treatments, and there is no cure, though there is evidence that antioxidants slow the rate of deterioration and the loss of vision. Vision loss is permanent. As yet there are no known measures to prevent ARMD. It appears that ARMD is more common in people who:

- smoke cigarettes
- have blue or green eyes
- experience extensive exposure to ultraviolet rays, as in sunlight exposure
- have CARDIOVASCULAR DISEASE (CVD) such as HYPERTENSION (high blood pressure), ATHEROSCLEROSIS, or CORONARY ARTERY DISEASE (CAD)

People who have more than one risk factor, especially when one of the risk factors is family history, should frequently and regularly monitor their vision using the Amsler grid. Early diagnosis is particularly important with wet ARMD, for which limited treatment options exist. ARMD develops in people over age 50. An ophthalmologist should evaluate changes that alter the field of vision, especially those that take the form of distortions or "missing pieces." Regular ophthalmic examinations are important to detect ARMD as well as other conditions that affect the eye and vision with advancing age.

See also AGING, VISION AND EYE CHANGES THAT OCCUR WITH; HEMORRHAGE; OPHTHALMIC EXAMINATION; RETINAL DETACHMENT; VISION HEALTH.

aging, vision and eye changes that occur with

The structures of the EYE and the processes of vision begin to undergo changes in the late fourth or early fifth decade of life. By age 65, 50 percent of people have vision impairments. By age 80, more than 90 percent of people have vision impairments. Treatment can mitigate some of these changes, such as PRESBYOPIA and CATARACT. Some conditions that affect the eye and vision develop secondary to other health conditions that are more prevalent in older people, such as DIABETES, HYPERTENSION, and KIDNEY disease, all of which can cause RETINOPATHY. Much loss of vision related to aging is progressive and permanent, interfering with activities such as driving, reading and other close work, and seeing at night. However, most people retain the ability to see well enough to function in everyday activities.

Adaptations to accommodate the changes of the eye and vision with aging are numerous and can help maintain a desirable QUALITY OF LIFE for many people. CORRECTIVE LENSES or reading glasses are effective for presbyopia. Surgery can improve vision impairments such as cataract (CATARACT EXTRACTION AND LENS REPLACEMENT), corneal damage (corneal reshaping or CORNEAL TRANSPLANTATION), and PTOSIS and ECTROPION (BLEPHAROPLASTY). Magni-

EYE CHANGES OF AGING AND THEIR EFFECTS ON VISION

Physical Change	Resulting Health Condition	Effect on Eyes or Vision
death of cones in the macula	AGE-RELATED MACULAR DEGENERATION (ARMD)	diminished VISUAL ACUITY in the center of vision
white rim around the CORNEA	arcus senilis	none
LENS cloudiness and discoloration	CATARACT	blurred or hazy vision; faded colors; progressive loss of vision
"STROKE" of the OPTIC NERVE that interrupts the flow of blood	ISCHEMIC OPTIC NEUROPATHY	diminished visual acuity; decreased VISUAL FIELD; progressive loss of vision
slowed chemical reactions in the rods	NIGHT BLINDNESS	diminished visual acuity in low-light circumstances
liquefaction of the vitreous humor	VITREOUS DETACHMENT	FLOATERS
loss of lens FLEXIBILITY	PRESBYOPIA	diminished ability to focus on near objects
atrophy (weakening) of the eyelid muscles and tissues, shifting of the orbital fat pads	PTOSIS; ECTROPION	partial occlusion of visual field; can cause CONJUNCTIVITIS, KERATITIS, CORNEAL INJURY

fiers for reading and close work, adjustments on televisions and computers to enlarge screen images, voice-activated telephone dialers, high-intensity light sources, and screen readers with voice output are among the devices available to accommodate low vision.

See also GENERATIONAL HEALTH-CARE PERSPECTIVES; VISION HEALTH.

amblyopia A VISION IMPAIRMENT, commonly called "lazy eye," in which the pathways between the EYE and the BRAIN do not properly handle the processes of sight. Amblyopia is most common in children. The impairment often develops when there are circumstances that allow one eye to become dominant in sending NERVE impulses to the brain, such as STRABISMUS (the inability of the eyes to focus on the same object) or congenital cataracts (opacity of the lens). Amblyopia can also develop when there is significant disparity in the refractive capabilities of the eyes, such as when one eye is hyperopic (farsighted) or myopic (nearsighted) and the other eye has normal vision. The brain becomes accustomed to messages the dominant eye and "ignores" nerve signals from the nondominant, or "lazy," eye. Untreated amblyopia can result in permanent vision impairment or legal blindness.

The diagnostic path includes close examination of the eyes to determine whether other disease processes are present that might account for the vision deficit. Treatment targets those processes, such as cataracts or REFRACTIVE ERRORS, when they exist. When the eye is otherwise healthy and normal, treatment consists of forcing the brain to rely on the amblyopic eye, usually by patching the dominant eye for structured periods of time. Sometimes the ophthalmologist will substitute atropine drops in the eye, which dilate the pupil and distort the eye's ability to focus, when a child refuses to wear an eye patch or an eye patch is otherwise not the most appropriate therapeutic choice. The dilation interferes with the eye's ability to focus, forcing the brain to interpret nerve messages from the untreated eye.

When detected and treated in children who are under age 9, most amblyopia responds to treatment and vision returns. Delayed or inadequate

treatment may result in permanent dysfunction of the eye–brain pathways, as these become entrenched by age 9 or 10. After this time the vision pathways are well established and amblyopia can no longer develop.

See also ASTIGMATISM; HYPEROPIA; MYOPIA; PTOSIS.

Amsler grid A basic test to detect or monitor the progression of AGE-RELATED MACULAR DEGENERATION (ARMD), a condition in which the macula, the area on the RETINA responsible for fine detail vision, deteriorates. The Amsler grid is a square with evenly spaced horizontal and vertical lines, and a dot in the center of the grid. The grid's four corners and lines should appear visible, straight, and intact. Wavy lines, gaps in the lines, or missing segments suggest damage to the macula. Such a result requires further examination from an ophthalmologist who specializes in retinal disorders.

See also VISUAL ACUITY.

astigmatism A common refractive error of vision that results from an irregularly shaped CORNEA. Astigmatism may affect one EYE or both eyes. Typically the irregularity results in two focal points of light that reach the RETINA instead of a single focal point, resulting in blurred or distorted images. Astigmatism often coexists with HYPEROPIA (farsightedness) or MYOPIA (nearsightedness) and tends to run in families. Corrective measures include eyeglasses, contact lenses, and REFRACTIVE SURGERY. Mild astigmatism may not produce noticeable vision disturbances, in which case it does not require correction. The success of corrective measures depends on the extent and nature of the corneal irregularities. Astigmatism often accompanies age-related changes in the eyes and vision, and is a common SIDE EFFECT of CORNEAL TRANSPLANTATION.

Less commonly astigmatism results from irregularities in the surface of LENS, called lenticular astigmatism. Options to correct for lenticular astigmatism are CORRECTIVE LENSES or lens-replacement surgery to implant an intraocular lens.

See also CATARACT EXTRACTION AND LENS REPLACEMENT; REFRACTION TEST; REFRACTIVE ERRORS.

B

black eye Bleeding into the tissues around the EYE resulting from trauma to the area, such as a blow or surgical OPERATION. As with any other bruise, the bleeding causes swelling and discoloration. The most significant concerns with a black eye are damage to the eye or fractures of the orbital bones, which require immediate medical attention.

Seek immediate medical attention if these symptoms accompany a black eye:

- **seeing dark spots (FLOATERS) or flashes of light**
- **any cuts on the insides of the eyelids or on the eye**
- **blurry, distorted, or double vision**
- **numbness on same side of the face**
- **trouble moving the eye to look up, down, or to either side**

Treatment for a simple black eye is cold to the area as quickly as possible after the injury occurs and at frequent intervals during the first 24 hours or until the PAIN subsides and the swelling stabilizes. A black eye may take two weeks to fully heal, and undergoes a number of color changes as HEALING progresses. People who participate in sports such as softball, baseball, basketball, tennis, racquetball, soccer, and similar events should wear appropriate eye protection.

See also BLEPHAROPLASTY; ORBITAL CELLULITIS; RETINAL DETACHMENT; RHINOPLASTY; TRAUMA TO THE EYE; VITREOUS DETACHMENT.

blepharitis INFLAMMATION of the eyelids. The most common causes of blepharitis are INFECTION and irritation. Anterior blepharitis is INFLAMMATION of the outer surface of the eyelid, typically along the rim at the base of the eyelashes. Posterior blepharitis affects the inner surface of the eyelid, typically resulting from blocked oil glands (meibomian glands) along the eyelid. Symptoms of either form of blepharitis may include

- itching or burning sensation
- crusting along the eyelids, especially upon awakening
- swelling and redness
- PHOTOPHOBIA (excessive light sensitivity)
- excessive tearing
- blurry vision

Blepharitis may develop as a result of other conditions such as DERMATITIS or ROSACEA (disorders that cause SKIN inflammation). When this is the case, treatment targets the underlying condition. When the cause of the inflammation is bacterial, treatment is topical and sometimes oral ANTIBIOTIC MEDICATIONS. Occasionally the viruses HERPES SIMPLEX I (which causes cold sores) and HERPES ZOSTER (which causes shingles) can infect the eyes. Viral infections such as these cause symptoms until they run their course, typically in 7 to 10 days. Whatever the cause of the inflammation, moist, warm compresses help loosen crusted secretions and keep the eyelids clean. EYE care professionals recommend gently washing the eyelids with a mixture of water and baby (tear-free) shampoo. Blepharitis tends to be chronic so good eyelid hygiene helps minimize recurrences as well as discomfort during episodes.

See also BACTERIA; CHALAZION; CONJUNCTIVITIS; DANDRUFF; DRY EYE SYNDROME; HORDEOLUM; ORBITAL CELLULITIS.

blepharoplasty A surgical OPERATION to remove excess tissue from the eyelids to correct drooping upper eyelids and "baggy" lower eyelids. Such conditions most commonly develop as a consequence of aging or extensive weight loss or when there is damage to the nerves that control the eyelid muscles (such as with PARKINSON'S DISEASE). An ophthalmologist or a plastic surgeon performs blepharoplasty, usually as an AMBULATORY SURGERY (also called outpatient or same-day surgery). Recovery takes two to four weeks; there can be significant swelling, bruising, and discoloration especially during the first two weeks after the operation. Cold compresses help reduce these symptoms. The risks of blepharoplasty include excessive bleeding and INFECTION.

See also BLACK EYE; BLEPHAROSPASM; PLASTIC SURGERY; PTOSIS; RHINOPLASTY; RHITIDOPLASTY; SURGERY BENEFIT AND RISK ASSESSMENT.

blepharospasm Involuntary closure of the eyelid that results from dysfunction of or damage to the nerves that control the muscles of the eyelids. Episodes of closure may range from brief (a minute) to extended (several hours). Extended closure interferes with vision. Doctors do not know what causes blepharospasm, though it is a symptom of numerous neurologic and neuromuscular disorders that affect MUSCLE control such as PARKINSON'S DISEASE and DYSTONIA. Blepharospasm that develops without an apparent underlying disorder is benign essential blepharospasm. Blepharospasm often begins with minor twitches and tics or squinting, progressing over time to forceful and prolonged contraction of the eyelid muscles. PHOTOPHOBIA (sensitivity to light) is common. Fatigue and CAFFEINE may initiate episodes of spasms.

The diagnostic path may include a NEUROLOGIC EXAMINATION to determine whether underlying neurologic disorders exist. Blepharospasm requires treatment when it begins to interfere with the activities of everyday life. Moderate blepharospasm often responds to MUSCLE RELAXANT MEDICATIONS such as clonazepam (Klonopin) or Lioresal (Baclofen), or to medications used to treat Parkinson's disease such as levodopa. Many people obtain long-term relief from injections of botulinum toxin, which temporarily paralyzes the eyelid muscles. Surgery to remove muscle tissue (myectomy) or to cut the nerves supplying the eyelid muscles (neurectomy) may provide relief. Though therapeutic measures can control symptoms, as yet there is no cure for blepharospasm.

See also BOTULINUM THERAPY; PTOSIS; SURGERY BENEFIT AND RISK MANAGEMENT; TIC.

blindness See VISION IMPAIRMENT.

braille A tactile (touch-based) system of written language that features patterns of raised dots to represent letters of the alphabet, common words and contractions, mathematical symbols, and punctuation. Named after its developer, Louis Braille (1809–1852), braille allows people who are blind to read and, with adaptive typewriters and computer technology, to write. Six dots, in two columns of three dots each, form the foundation for braille; the presence or absence of dots in specific patterns identifies the letter, number, symbol, or concept. There are a number of braille variations, or codes, in common use in the United States. The major ones are these:

- American literary braille code uses about 250 patterns to create book-length materials using short-form words, contractions, single-cell words, and symbols; patterns may have multiple meanings interpreted by context.
- Grade 2 braille code is an abbreviated variation of American literary braille code used primarily for recreational reading materials such as novels and nonacademic nonfiction.
- Grade 1 braille code is the basic alphabet and numerals 0 through 9.
- Nemeth braille code contains about 600 unique, specialized patterns that are distinct from American literary braille code for use in mathematics and science.
- Computer braille code provides a mix of American literary braille code, Nemeth braille code, and unique symbols for computer programming and instruction documentation.
- Music braille code is specialized for transcribing musical scores.

Learning each variation of braille code is like learning a different language. Most people learn the one or two variations they are most likely to use. People whose vision is intact also can learn braille, and should if they have regular interactions with people who are blind. Many communities have schools and consultants who teach braille as well as libraries that provide braille publications. Most public signage in the United States includes braille translations.

See also VISION IMPAIRMENT.

bullous keratopathy Swelling (edema) and blistering of the CORNEA. Bullous keratopathy most commonly develops as a complication following CATARACT EXTRACTION AND LENS REPLACEMENT or other surgery on the EYE, though it also may develop as a consequence of chronic irritation such as might occur with DRY EYE SYNDROME.

The healthy cornea is about 75 percent water. One function of the cells that surround the cornea is to maintain this fluid balance. Irritation and trauma that damage these cells diminishes their ability to function, and the cornea retains more water. The swelling stretches the surface of the cornea, pushing the cornea into closer contact with the eyelid and resulting in further irritation. Bullae, or blisters, develop as the cornea's attempt to relieve the discomfort, much as blisters develop on the feet or hands in reaction to friction.

Early symptoms of bullous keratopathy are a sensation of grittiness in the eye, blurred vision, excessive tearing, and PHOTOPHOBIA (sensitivity to light). When bullae form, and especially when they rupture, the PAIN often is severe. The ophthalmologist can diagnose bullous keratopathy using SLIT LAMP EXAMINATION of the cornea, a painless procedure that combines an intense light focused in a slit with magnification through a ophthalmologic microscope. Eye drops or ointment with a higher saline concentration than tears helps draw fluid out of the cornea, reducing the swelling. Soft contact lenses, which absorb fluid from the eye and shield the cornea from contact with the eyelid, relieve discomfort for many people. Bullous keratopathy tends to be chronic, and over time may result in damage to the cornea that requires the cornea's surgical removal (keratotomy) or CORNEAL TRANSPLANTATION.

See also BLISTER; KERATITIS; UVEITIS.

C

cataract Cloudiness and discoloration of the LENS. Cataracts become increasingly common with advancing age, affecting half of all people age 80 and older. Cataracts were once a leading cause of age-related blindness. Today ophthalmologists surgically remove cataracts and replace the lens with a prosthetic intraocular lens (IOL) that restores vision.

Cataracts result from protein deposits that accumulate within the lens. These deposits disperse light in much the same way cracks in a window might splinter sunlight shining through. The fragmented light creates areas of accentuated brightness, causing the halos and sensitivity to lights at night. The opacity of the cataract interferes with the refractive function of the lens, causing blurry or hazy vision. The yellow or gray discoloration of the lens common with mature or "ripe" cataracts filters the lightwaves that enter the EYE, particularly affecting those in the spectrum of blue. The location of the cataract on the lens determines the nature and extent of VISION IMPAIRMENT.

Age-related cataracts Most cataracts develop as a function of aging. Protein structures within the body, including the lens of the eye, begin to change. The lens becomes less resilient. Such changes make it easier for proteins to clump together, forming areas of opacity that eventually form cataracts. Nuclear cataracts form in the nucleus (gelatinous center) of the lens and are the most common type of age-related cataract. Cortical cataracts form in the cortex, or outer layer, of the lens and often do not affect vision.

Congenital cataracts Infants may be born with cataracts. A congenital cataract affecting only one eye typically is idiopathic (without identifiable cause); congenital cataracts affecting both eyes often suggest genetic disorders such as DOWN SYNDROME. A congenital cataract that is in the line of vision (on the visual axis) can cause significant vision impairment or blindness because the pathways for vision develop in the infant's first few months of life. Ophthalmologists usually remove such cataracts as soon as possible. Other congenital cataracts may be small and located so they are inconsequential to vision; ophthalmologists generally take an approach of watchful waiting with these.

Cataracts of diabetes GLUCOSE, which can be present in high blood levels with DIABETES, interacts with the protein structure of the lens, causing protein clumping. People who have type 1 (INSULIN-dependent) diabetes are at greatest risk for cataracts of diabetes, which often develop at a young age. People who have type 2 diabetes or insulin resistance also are at increased risk. Developing cataracts account in part for the vision disturbances that are among the symptoms of diabetes. Treatment for cataracts of diabetes is the same as for age-related cataracts.

Symptoms and Diagnostic Path

Because cataracts develop slowly, symptoms become gradually noticeable. Symptoms usually affect only one eye (though cataracts may develop concurrently in both eyes) and may include

- blurry or hazy vision
- double vision
- halos around lights at night
- difficulty seeing at night
- colors appearing faded or dull, or difficulty perceiving shades of blue and purple

Gradual loss of vision at middle age and beyond may be a symptom of AGE-RELATED MACULAR DEGENERATION (ARMD) or GLAUCOMA. Untreated, these conditions result in significant and permanent vision impairments. Any decrease in vision requires an ophthalmologist's or optometrist's prompt evaluation.

The ophthalmologist can see cataracts during OPHTHALMOSCOPY, a painless procedure for examining the interior of the eye.

Treatment Options and Outlook

CATARACT EXTRACTION AND LENS REPLACEMENT is the treatment of choice for nearly all cataracts. There is no element of time-sensitivity for the surgery. Though VISUAL ACUITY will progressively deteriorate as the cataract enlarges, there is no permanent harm to vision by waiting to extract the cataract. Following cataract surgery, more than 90 percent of people experience vastly improved vision. Some people who are unable to receive an IOL because of other eye conditions will need to wear a special contact lens or eyeglasses to carry out the refractive functions of the extracted lens. Nearly everyone will still need reading glasses to accommodate PRESBYOPIA.

Risk Factors and Preventive Measures

Cataracts are primarily a consequence of aging. Cataracts also can develop as a SIDE EFFECT of long-term STEROID use (therapeutic or performance enhancing). Cigarette smoking, excessive ALCOHOL consumption, and extended exposure to sunlight (ultraviolet rays) are among the lifestyle factors associated with early or accelerated cataract development. There are no known methods for preventing cataracts.

See also AGING, EYE AND VISION CHANGES THAT OCCUR WITH; ANABOLIC STEROIDS AND STEROID PRECURSORS; CORTICOSTEROID MEDICATIONS; SMOKING AND HEALTH.

cataract extraction and lens replacement An OPERATION to remove the LENS from the EYE after a CATARACT (cloudy occlusion in the lens) forms and replace it with a prosthetic intraocular lens (IOL). Ophthalmologists can extract a cataract at any stage of its development. The vast majority of people who undergo cataract extraction fully recover without complications and experience VISUAL ACUITY correctable to 20/40 or better.

Surgical Procedure

Cataract extraction is nearly always an outpatient surgery performed under local anesthetic and a mild general sedative for comfort. There are three surgical procedures for cataract extraction. Each takes 20 to 30 minutes for the ophthalmologist to complete. Many variables influence the ophthalmologist's choice for which to use.

Phacoemulsification The most commonly performed cataract extraction procedure is phacoemulsification, which requires a tiny incision into the capsule containing the lens. The ophthalmologist first uses ULTRASOUND to liquefy the central nucleus (inner, gelatinous portion of the lens) and then uses aspiration to remove it. Last the ophthalmologist removes the cortex (outer layer of the lens) from the capsule in multiple segments.

Extracapsular cataract extraction The extracapsular cataract extraction procedure requires a slightly larger incision in the capsule, through which the ophthalmologist removes the central nucleus of the lens intact, then removes the cortex in multiple segments.

Lens replacement After extracting the cataract, the ophthalmologist inserts either a monofocal or multifocal IOL to give the eye the ability to focus. Contemporary lens designs allow the ophthalmologist to fold the lens, insert it into the lens capsule through the tiny incision used to extract the cataract, and unfold the IOL to place it in position.

BENEFITS AND RISKS OF CATARACT EXTRACTION

Benefits	Risks
restores vision	postoperative PAIN and swelling (uncommon)
improves QUALITY OF LIFE	postoperative INFECTION (uncommon)
	RETINAL DETACHMENT (rare)

Risks and Complications

Most ophthalmologists prescribe antibiotic and anti-inflammatory eye drops applied to the eye for four to six weeks following surgery, and recom-

mend wearing dark glasses in bright light to help protect the eye from light sensitivity. Swelling and irritation of the tissues around the operated eye is normal in the first few weeks following surgery. Clear vision may take four to six weeks, though many people experience dramatic improvement immediately. Though the short-term risks of cataract extraction and lens replacement are minor, RETINAL DETACHMENT can occur months to years following surgery.

Cataract extraction is a permanent solution for cataracts. Once removed, cataracts cannot grow back. Some people do develop a complication called posterior capsule opacity, in which the membrane behind the IOL becomes cloudy (opaque). This is a complication that results when residual cells that remain after removal of the lens begin to grow across the membrane, causing the membrane to thicken. A follow-up procedure, either yttrium-aluminum-garnet (YAG) laser capsulotomy or conventional surgery, is necessary to remove the membrane.

Outlook and Lifestyle Modifications

About 90 percent of people experience vastly improved vision after cataract extraction. However, other eye problems or underlying conditions (such as RETINOPATHY of diabetes) can affect the quality of vision. Many people do need eyeglasses after cataract extraction, as the IOL does not adjust for focus as does a natural lens. It is important to see the ophthalmologist for follow-up and routine eye care as recommended.

See also AGE-RELATED MACULAR DEGENERATION (ARMD); BULLOUS KERATOPATHY; HYPEROPIA; MYOPIA; PRESBYOPIA; SMOKING AND HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT.

chalazion A painless, hard nodule that arises from a gland (meibomian or sebaceous) along the edge of the eyelid, the result of glandular secretions that granulate. A chalazion may extend deep into the structure of the eyelid. A chalazion sometimes forms at the site of a recurrent HORDEOLUM (an infected eyelid SEBACEOUS GLAND, also called a stye). Often a small chalazion will go away on its own, without treatment. Moist heat applied to the eyelid helps dissolve the granulated material and draw it from the gland. Because of the risk of scarring and pain, the ophthalmologist may recommend excising (surgically removing) a chalazion that does not go away or that recurs. The procedure, with local anesthetic to numb the eyelid, takes only a few minutes in the doctor's office. The wound typically heals within two weeks and leaves no scarring. Inflammatory skin conditions such as DERMATITIS or ROSACEA can block the eyelid's glands, causing a chalazion to develop. Careful eyelid hygiene helps keep secretions from accumulating.

See also BLEPHARITIS; CONJUNCTIVITIS; OPERATION.

cicatricial pemphigoid An autoimmune disorder in which painful blisters form on the inner surfaces of the eyelids (and may form on other mucus membranes, such as in the MOUTH and NOSE). SCAR tissue that forms after the blisters heal continues to irritate the inner eyelids as well as the outer surface of the EYE (sclera and CORNEA). The blisters commonly involve the lacrimal (tear) glands and ducts, reducing tear production and causing DRY EYE SYNDROME. Cicatricial pemphigoid occurs when the body's IMMUNE SYSTEM produces antibodies that attack the cells that form the mucus membranes. Trauma appears to activate the eruptions of blisters and may be as inconsequential as rubbing the eye or the irritation such as occurs with exposure to environmental particulates such as pollen and dust. Some people first experience outbreaks of cicatricial pemphigoid following eye operations such as CATARACT EXTRACTION AND LENS REPLACEMENT or BLEPHAROPLASTY.

The diagnostic path includes laboratory tests to assess the levels of antibodies in the blood, particularly IMMUNOGLOBULIN G (IGG) and IMMUNOGLOBIN A (IGA), the antibodies most closely associated with cicatricial pemphigoid. Treatment focuses on reducing BLISTER formation and minimizing scarring, typically by taking oral CORTICOSTEROID MEDICATIONS or IMMUNOSUPPRESSIVE MEDICATIONS. As with other AUTOIMMUNE DISORDERS, cicatricial pemphigoid tends to be chronic and recurrent. The persistent irritation can result in damage to the cornea that causes VISUAL IMPAIRMENT and, when severe, results in blindness.

See also ANTIBODY; CONJUNCTIVITIS; CORNEAL TRANSPLANTATION; ECTROPION; HUMAN LEUKOCYTE ANTIGEN (HLA).

color deficiency A VISION IMPAIRMENT in which the ability to distinguish certain, and rarely all, colors is impaired. Color deficiency represents a shortage of normal cones, the specialized cells on the RETINA that detect color. Cones contain photosensitive chemicals that react to red, green, or blue. The most common presentation of color deficiency, accounting for about 98 percent of color deficiency, is red/green deficiency, in which the person cannot distinguish red and green. A small percentage of people cannot distinguish blue and yellow. Rarely, a person sees only in shades of gray.

Color perceptions occur when lightwaves of certain frequencies (lengths) activate the photochemicals in cones that are sensitive to the frequency. The BRAIN interprets the varying intensities and blends of the photochemical responses. Color deficiency occurs when the cones that perceive one of the three primary colors (red, green, blue) do not function properly.

The most common test for color vision and color deficiency is a series of disks that contain dots of color in random patterns with a structured pattern of differing color within the field. The structured pattern may be a number (most commonly) or an object. There is no treatment to compensate for color deficiency. People who are color-deficient learn to accommodate the deficiency through mechanisms such as memorizing the locations of colored objects (such as the sequence of lights in a traffic signal) and by making adaptations in their personal environments. A person may have friends or family members sort clothing by color, for example, and label the color groups. Some people who have mild color deficiency experience benefit from devices such as colored glasses and colored contact lenses that filter the lightwaves that enter the EYE. A yellow tint may improve blue-deficient color vision, for example.

Most color deficiency is an X-linked genetic MUTATION, affecting about 8 percent of men and ½ percent of women. Color deficiency may also develop with AGE-RELATED MACULAR DEGENERATION (ARMD), RETINOPATHY, neurologic disorders such as MULTIPLE SCLEROSIS, and HEAVY-METAL POISONING such as lead or mercury. Antimalarial drugs can cause permanent changes in the RETINA that affect color vision; the ERECTILE DYSFUNCTION medication sildenafil (Viagra) can temporarily intensify the perception of blue.

See also VISION HEALTH; VISUAL ACUITY.

conjunctivitis An INFLAMMATION of the conjunctiva, or mucous tissue that lines the inside of the eyelids. There are many causes for conjunctivitis, commonly called pink EYE, including INFECTION (bacterial, viral, or fungal) and contact contamination such as due to pollen or substances in the air or on the fingers that irritate the tissues. Infectious conjunctivitis is highly contagious and very common, especially in children. Symptoms include

- red, swollen conjunctiva and sclera (inner eyelids and the "white" of the eye)
- itchy or scratchy sensation
- thick, yellowish discharge that crusts
- PHOTOPHOBIA (sensitivity to light)

The doctor can usually diagnose conjunctivitis from its appearance. Typical treatment is application of an antibiotic medication in ophthalmic preparation (drops or ointment). Most conjunctivitis dramatically improves with 48 hours of initiating treatment, though symptoms may resolve gradually over 10 to 14 days, and does not require further medical attention. The doctor may culture the discharge when there is reason to suspect CHLAMYDIA or GONNORHEA is the cause, or when symptoms do not improve with treatment. Warm, moist compresses help relieve discomfort and clear away the discharge. Frequent HAND WASHING helps prevent spreading the infection. Untreated conjunctivitis, particularly when chlamydia or gonorrhea is the infectious agent, can cause permanent damage to the CORNEA, which results in VISUAL IMPAIRMENT or blindness.

See also ALLERGIC CONJUNCTIVITIS; ANTIBIOTIC MEDICATIONS; BACTERIA; FUNGUS; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; VIRUS.

cornea The transparent portion of the sclera, the EYE's outer layer. The cornea functions as a window to allow light to enter the eye and is the first point of refraction (bending lightwaves to focus them on the RETINA). Irregularities in the surface of the cornea can distort refraction, resulting in

ASTIGMATISM. Though the cornea has no BLOOD vessels it has numerous NERVE endings that make it highly sensitive. Because it is the outermost portion of the eye, the cornea is also highly vulnerable to injury.

For further discussion of the cornea within the context of ophthalmologic structure and function please see the overview section "The Eyes."

See also CORNEAL INJURY; CORNEAL TRANSPLANTATION; LENS; REFRACTIVE ERRORS.

corneal injury Lacerations, punctures, and blunt trauma to the CORNEA. Because of its position, somewhat protruding at the front of the EYE, the cornea is at risk for damage that can jeopardize vision.

Corneal injuries require immediate medical attention. Any puncture or penetrating wound to the eye is a medical emergency. Loosely patch *both* eyes to minimize eye movement.

Dust, dirt, pollen, and other particulates in the air can scratch the surface of the cornea. Particles that adhere to the inside of the upper eyelid or objects that slash across the cornea before the eyelid reflexively closes may cause lacerations (cuts) to the cornea. Though the cornea has no blood vessels and thus cannot bleed, it has numerous nerve endings that unmistakably sound the alert when injury occurs. Injury to the cornea also can diminish VISUAL ACUITY. Puncture or penetrating injuries can destroy the cornea and expose the inner eye to traumatic damage as well as INFECTION. Even minor ABRASIONS and lacerations can cause temporary vision impairment as well as present the risk for infection. Loss of the eye is possible when a significant penetrating wound allows the inner contents of the eye to escape.

Symptoms of corneal injury include

- discomfort ranging from a scratchy sensation to frank PAIN
- PHOTOPHOBIA (sensitivity to light)
- excessive tearing
- inability to keep the eye open
- blurred or distorted vision

The ophthalmologist can identify a corneal injury with FLUORESCEIN STAINING, a simple and painless procedure. Any areas of injury on the cornea absorb the fluorescein dye, causing them to glow green under blue light. Serious injuries to the cornea, or embedded foreign objects, may require immediate surgery to minimize loss of vision. Treatment for injuries that affect only the surface of the cornea may include ophthalmic ANTIBIOTIC MEDICATIONS (drops or ointment) and patching of the affected eye. Protective eyewear, worn whenever there is the potential for particles or objects to strike the eye, helps prevent corneal injuries.

See also CORNEAL TRANSPLANTATION; TRAUMA TO THE EYE.

corneal transplantation The replacement of a diseased CORNEA with a healthy donor cornea. In the United States, ophthalmologists perform more than 45,000 corneal transplantations each year; up to 90 percent of people who receive transplanted corneas experience restored vision; success depends on the reason for the transplant. Ophthalmologists may recommend corneal transplantation to treat:

- BULLOUS KERATOPATHY
- KERATOCONUS
- KERATITIS
- significant CORNEAL INJURY

Donor corneas are harvested within a few hours of death and can be preserved for up to 14 days. Current practice does not employ blood type or tissue type matching for corneal transplantation, though some studies suggest matching the blood type of donor and recipient reduces the risk for rejection.

CORNEA DONATION

Nearly anyone can donate his or her corneas after death. There is no cost to the donor. An eye bank coordinates the harvesting, testing, storage, and dispensing of donated corneas. Many states incorporate organ donor authorization with driver's licenses. People should tell family members that they wish to donate their corneas.

Corneal transplantation surgery takes place with a local anesthetic to numb the eye and an intravenous sedative medication for relaxation and comfort. The operation takes 45 to 60 minutes. From the donor cornea, the ophthalmologist uses a trephine, a device that cleanly punches out a buttonlike segment of the cornea's center. Using a surgical microscope, the ophthalmologist then removes a similarly shaped segment from the diseased cornea and places the donor button in its place. Very fine suture, sometimes thinner than a human hair, secures the donor corneal button in position and remains in the eye for three months to one year. The ophthalmologist often removes the sutures a few at a time as HEALING progresses, using an ophthalmic anesthetic to numb the affected eye, depending on the rate of vision improvement. Some sutures may remain in place indefinitely.

Full recovery typically takes about a year. Some people will have ASTIGMATISM and require CORRECTIVE LENSES following corneal transplantation, resulting from irregularities in the shape of the cornea that develop during healing. Corneal transplantation may correct another VISION IMPAIRMENT such as HYPEROPIA (farsightedness) or MYOPIA (nearsightedness) because the OPERATION changes the shape of the cornea.

The most common complication of corneal transplantation is rejection of the transplanted cornea, which occurs overall in about 15 percent of corneal transplantations. Rejection is most likely to take place in the first two years after the operation. Early detection and prompt treatment with ophthalmic CORTICOSTEROID MEDICATIONS can reverse the rejection process. Signs of rejection include

- diminished VISUAL ACUITY
- PAIN
- redness of the eye
- PHOTOPHOBIA (sensitivity to light)

Other complications that can occur include INFECTION and bleeding within the eye.

See also ORGAN TRANSPLANTATION; PHOTOTHERAPEUTIC KERATECTOMY (PTK).

corrective lenses Eyeglasses or contact lenses that alter the focal point of the lightwaves entering the EYE to correct REFRACTIVE ERRORS of vision, including HYPEROPIA (farsightedness), MYOPIA (nearsightedness), ASTIGMATISM (blurred or distorted vision), and PRESBYOPIA (age-related hyperopia). The eye's natural focusing structures, the CORNEA and the LENS, gather lightwaves and refract (bend) them toward their centers. The cornea refracts the lightwaves first. The lens, which can thicken or flatten to refine its focal efforts, refracts the somewhat focused lightwaves that come to it from the cornea. In normal vision, this sequence results in the focal point of the lightwaves striking the RETINA.

When refractive errors exist the focal point falls in front of or behind the retina, resulting in blurred images. Corrective lenses add a third level of refraction to compensate for the error, bending the lightwaves before they enter the cornea to realign their focal point. The direction of refraction depends on the refractive error:

- In myopia, the focal point falls short of the retina. A lens that corrects for myopia bends the lightwaves inward, narrowing the span of light as it enters the cornea to lengthen the focal point. Such a lens is thicker at the edges than in the middle (concave); it is a minus spherical correction.
- In hyperopia, the focal point extends beyond the retina. A lens that corrects for hyperopia bends the lightwaves outward, broadening the span of light as it enters the cornea to shorten the focal point. Such a lens is thicker in the center than at the edges (convex); it is a plus spherical correction.
- In astigmatism, irregularities in the surface of the lens cause a second focal point. A lens that corrects for astigmatism refracts along a specific axis, realigning the lightwaves. This is a cylinder correction.

Corrective lenses can, and often do, combine spherical and cylindrical corrections. A multifocal lens further incorporates a correction for presbyopia in the form of a bifocal, trifocal, or progressive lens. The bottom of the lens is a plus section,

added to the corrective prescription, that accommodates the limited ability of the lens to focus on near objects (such as when reading).

Eyeglasses

Eyeglasses are plastic resin or polycarbon, and less commonly glass, lenses ground to the thicknesses and shapes necessary to achieve the desired refractive specifications. Because eyeglasses are external to the eye, they can correct for a broad range of refractive errors and are the most common means of refractive correction. Eyeglasses also can contain tints and dyes that change their color; some have additives that provide protection from ultraviolet light. About 85 percent of people who have refractive errors of vision wear eyeglasses to correct them.

Bifocal and trifocal eyeglasses have a clear shift (sometimes visible as a line on the lens) to the presbyopic correction; a progressive lens transitions to the presbyopic correction. Reading glasses such as those available without an eye care practitioner's prescription, are magnifying lenses that enlarge close objects, requiring the lens to make less of an adjustment to bring them into focus. How well reading glasses work depends on whether there are refractive errors that remain uncorrected. With aging, most people develop at least a small degree of astigmatism, which can result in blurred or distorted images not related to presbyopia.

The primary risk of wearing eyeglasses is traumatic injury due to a blow that strikes the glasses. The energy of such a blow concentrates initially at the contact points on the NOSE. The frame may break, causing lacerations to the face. Of more significant consequence is a blow that breaks the lens, which can result in vision-threatening injury to the eye. Polycarbonate lenses have the highest inherent shatter resistance; plastic resin and glass lenses should have shatter-resistant coatings or additives. People who engage in physical activities such as ball sports should wear polycarbonate eyeglasses or custom protective eyewear.

Contact Lenses

Contact lenses fit directly onto the eye, covering the cornea. There are two basic kinds of contact lenses in use today: gas permeable (hard) and hydrophilic (soft). Gas-permeable contact lenses float on a layer of tears over the center of the cornea and often are the contact lens of choice to correct for moderate to significant astigmatism as well as KERATOCONUS, a condition in which the cornea's center bulges outward. Gas-permeable lenses also can correct for mild to moderate myopic and hyperopic refractive errors. Made of rigid polymers of fluorocarbon and polymethyl methacrylate, gas-permeable lenses allow oxygen molecules to pass through but do not absorb moisture from the eye. Hydrophilic contact lenses cover the entire cornea and can correct for mild to moderate myopia and hyperopia. Soft and flexible, hydrophilic lenses contain a high percentage of water and draw additional moisture from the tears to remain hydrated. A special kind of hydrophilic lens, the toric lens, is necessary to correct for astigmatism. A toric lens has varying thicknesses that compensate for corneal irregularities to correct refraction.

Contact lenses can incorporate correction for moderate presbyopia, though this tends to be a less satisfactory approach than eyeglasses. There are two methods for accommodating presbyopia with contact lenses: progressive or bifocal lenses and monovision. Progressive or bifocal contacts function much the same as progressive or bifocal eyeglasses, with the lower portion of the lens containing the presbyopic correction. Because contact lenses shift position on the eye with blinking and when the wearer alters the angle of the head (such as when lying down), the presbyopic correction may not remain in an effective position. Monovision takes the approach of modifying the BRAIN's interpretation of visual signals. One eye, usually the dominant eye, wears a contact lens with the refractive correction. The other eye wears a contact lens with the presbyopic correction. The brain learns to distinguish which signals to interpret, accepting those from the dominant eye during normal visual activities and those from the other eye when reading or doing close-focus work.

The primary risks of wearing contact lenses are damage to the cornea and INFECTION. Even hydrophilic lenses can irritate the cornea and

cause corneal ABRASIONS, particularly in dusty, windy, or dry environmental conditions. Contact lenses tend to accumulate protein deposits that cause irritation. Most hydrophilic lenses are disposable, so frequent replacement helps minimize this as a problem. The optician may need to clean or gently grind the surface of gas-permeable lenses to clear away deposits. Contact lens hygiene, including diligent HAND WASHING before handling lenses and storing lenses in the appropriate disinfectant solution, is essential.

Reading a Corrective Lens Prescription

Optometrists and ophthalmologists measure refractive errors in diopters, a representational scale of the distance in front of or behind the eye's lens the focal point of lightwaves entering the eye must shift to allow the light waves to clearly focus on the retina. The larger the diopter number, the more the lens refracts, or bends, the light. A corrective lens prescription represents the diopter as minus or plus, according to the direction the correction shifts the focal point. For example, the following prescription corrects for myopia and astigmatism:

OD	– 5.75	+ 0.50	164
OS	– 6.00	+1.75	115

This prescription denotes different refractive corrections for the right eye (OD) and left eye (OS). The minus diopter is the spherical correction for the myopia; the plus diopter is the cylindrical correction for the astigmatism, and the last number is the axis position for the cylindrical correction. A lens with a strong correction may also include an adjustment that tilts the lens to alter its optical center, the prism, allowing a thinner lens to deliver the same corrective power or to accommodate a significant difference in the refractive correction for each eye (anisometropia).

See also REFRACTION TEST; REFRACTIVE SURGERY; VISION IMPAIRMENT.

D

dacryocystitis INFLAMMATION of the lacrimal (tear) ducts, typically the nasolacrimal ducts in the corners of the EYE near the NOSE. Dacryocystitis develops when there is a blockage of the lacrimal duct, which may result from DACRYOSTENOSIS (narrowing of the lacrimal duct), INFECTION, or chronic irritation such as might occur with ALLERGIC RHINITIS or ALLERGIC CONJUNCTIVITIS. Dacryocystitis can be acute (of sudden onset) or chronic (recurrent or long-standing). It also can be congenital (the result of defects of the lacrimal gland and duct structures) or acquired. Most people who have acquired dacryocystitis are over age 65.

Common symptoms include

- redness and swelling between the eye and the bridge of the nose
- rhinitis (runny nose)
- PAIN
- overflowing tears
- FEVER when an infection is present

The doctor can typically diagnose dacryocystitis based on its presentation. Dye tests, in which the doctor places a special dye in the eye and watches to see whether the dye discolors nasal discharge, help identify the extent of blockage causing the inflammation. Treatment includes ANTIBIOTIC MEDICATIONS when there is an infection, or procedures to dilate the lacrimal duct when there is no infection. Sometimes surgery is necessary to correct dacryostenosis or other structural defects. Appropriate treatment resolves the dacryocystitis.

See also BLEPHARITIS; EYE PAIN; OPERATION; ORBITAL CELLULITIS.

dacryostenosis Narrowing of the lacrimal (tear) duct, usually congenital, that blocks the flow of tears. An infant does not produce a great volume of tears during the first few weeks to months after birth, so the doctor may not suspect or diagnose dacryostenosis until the infant is three to four months of age. The most common symptom is tears that overflow the eye and run down the face (epiphora). Most infants outgrow dacryostenosis by age six months, so doctors tend to take an approach of watchful waiting. When dacryostenosis persists, the doctor may dilate the lacrimal duct (under anesthetic) to gently stretch and enlarge the opening for tears to pass unimpeded. Untreated dacryostenosis can result in frequent episodes of DACRYOCYSTITIS (infected lacrimal ducts) in adulthood. Appropriate treatment can completely resolve dacryostenosis.

See also INFECTION; ORBITAL CELLULITIS.

dark adaptation test A test that assesses the ability to see in a dimly lighted environment. There are several ways to perform a dark adaptation test. One of the most common is to have the person sit in a dimly lit room. The examiner shines a light into the EYE, gradually increasing the light's intensity until the person reports seeing the light. The examiner notes the light's intensity and the length of time it takes for the light to become noticeable. Depending on the reason for the test, the examiner may direct the light to different parts of the RETINA to test the responsiveness of the rods (the cells responsible for low-light vision). A decrease in dark adaptation response is normal with aging as the photochemical reactions in the eye slow.

See also AGING, VISION AND EYE CHANGES THAT OCCUR WITH; ELECTRORETINOGRAPHY; NIGHT BLINDNESS; RETINITIS PIGMENTOSA; RETINOPATHY.

diplopia The medical term for double vision, a circumstance in which a person perceives a single object as a two distinct images. Diplopia can be vertical (images one above the other) or horizontal (images beside each other). Diplopia that is present when using both eyes and goes away when covering one EYE is binocular; diplopia that persists even when one eye is covered is monocular. Each has different clinical implications. Numerous health conditions can cause diplopia or have diplopia among their symptoms.

Causes of Monocular Diplopia	Causes of Binocular Diplopia
ASTIGMATISM	BRAIN injury (traumatic or STROKE)
CATARACT	BRAIN TUMOR
DRY EYE SYNDROME	DIABETES
KERATOCONUS	cranial NERVE disorders
PTERYGIUM	GRAVES'S OPHTHALMOPATHY
RETINOPATHY	MULTIPLE SCLEROSIS
STRABISMUS	MYASTHENIA GRAVIS

The diagnostic path begins with basic OPHTHALMIC EXAMINATION and NEUROLOGIC EXAMINATION. The findings of these exams determine the direction and nature of further testing. As diplopia is a symptom rather than a condition, treatment targets the underlying cause. In degenerative disorders such as MULTIPLE SCLEROSIS and MYASTHENIA GRAVIS, diplopia may persist or worsen as the condition progresses. For monocular diplopia, patching the affected eye may alleviate the double image.

See also AMBLYOPIA; CRANIAL NERVES; STRABISMUS; VISION IMPAIRMENT.

dry eye syndrome A condition in which the lacrimal (tear) glands do not produce enough tears or the tears evaporate too quickly, causing the EYE to become dry and irritated. Dry eye syndrome has numerous causes, the most common of which are aging, medication side effects, and extended exposure to a dry or dusty environment. People who work in occupations that require close focus, such as with computers or assembly-line tasks, also may develop dry eyes as a result of insufficient blinking. Dry eyes also may accompany autoimmune conditions such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), RHEUMATOID ARTHRITIS, and SJÖGREN'S SYNDROME. Cigarette smoking exacerbates dry eye syndrome.

The symptoms of dry eye syndrome include redness, itching, and the sensation of grit in the eyes. The diagnostic path targets identifying the underlying cause when possible. ANTIHISTAMINE MEDICATIONS, antihypertensive medications, ANTIDEPRESSANT MEDICATIONS, and medications to treat PARKINSON'S DISEASE commonly cause dry eyes as a SIDE EFFECT; sometimes switching to a different medication reduces eye dryness and irritation.

Treatment is frequent use of artificial tears or restasis drops and remedying any identifiable cause when possible. The ophthalmologist may treat persistent dry eye syndrome with lacrimal plugs (also called punctal plugs), tiny segments of acrylic that become soft and gelatinous when inserted into the lacrimal ducts. These plugs slow the drainage of tears from the eye. Some recent studies suggest that increasing dietary intake of essential fatty acids, notably linoleic and gamma-linolenic acids, improves the eye's ability to produce tears.

See also AGING, VISION AND EYE CHANGES THAT OCCUR WITH; ALLERGIC CONJUNCTIVITIS; ALLERGIC RHINITIS; BLEPHARITIS; CONJUNCTIVITIS.

E

ectropion Loss of elasticity or control of the eyelid, usually the lower eyelid, that causes it to sag away from the EYE. Ectropion allows tears to overflow the lid rather than remaining in the eye. It also fails to protect the eye, and especially the CORNEA, permitting dryness and exposure to environmental particles that create irritation and possibly injury to the cornea and sclera ("white" of the eye). Common causes of ectropion include

- aging
- damage to the nerves that control the eyelids
- CICATRICIAL PEMPHIGOID

Ectropion is a common symptom of BELL'S PALSY, a temporary paralysis of one side of the face that results from INFLAMMATION of the seventh cranial NERVE (facial nerve), and also may accompany neurologic disorders such as PARKINSON'S DISEASE and MULTIPLE SCLEROSIS.

With ectropion the eye feels irritated and scratchy. Tear production becomes excessive as the eye attempts to lubricate and protect itself, and tears typically run over the lip of the lid and onto the cheeks. The doctor can diagnose ectropion based on its appearance. Treatment is typically surgery to tighten the lid structure to permit the lid to stay against the eye. Whether the ectropion recurs depends on the underlying cause. Untreated ectropion may result in extensive damage to the surface of the eye and cornea, including INFECTION, that interferes with vision and the health of the eye.

See also AGING, VISION AND EYE CHANGES THAT OCCUR WITH; CONJUNCTIVITIS; CORNEAL INJURY; CRANIAL NERVES; ENTROPION; KERATITIS.

electroretinography A test that measures the electrical activity of the RETINA's rods and cones in response to light stimulation. The ophthalmologist places anesthetic drops in the EYE to numb it, then attaches an electrode to the surface of the CORNEA. The electrode detects electrical impulses on the retina when the ophthalmologist flashes a beam of light onto the retina, and sends signals to the electroretinograph machine. An electroretinogram is the recording the machine makes of the retina's responses. Electroretinography helps diagnose disorders of the retina such as RETINAL DETACHMENT and RETINITIS PIGMENTOSA.

See also DARK ADAPTATION TEST; RETINOPATHY; SLIT LAMP EXAMINATION.

entropion Deformity of the eyelid in which the lip of the lid, including the eyelashes, curls inward toward the EYE. Scarring that results from CICATRICIAL PEMPHIGOID (an AUTOIMMUNE DISORDER in which painful blisters repeatedly form on the insides of the eyelids) or recurrent CONJUNCTIVITIS (INFLAMMATION or INFECTION of the inner lining of the eyelids) is a common cause of entropion. Entropion may also develop for unknown reasons (idiopathic). The ophthalmologist can diagnose entropion by its presentation. The irritation of the lid and lashes against the surface of the eye is painful and can cause significant damage to the CORNEA, resulting in VISION IMPAIRMENT and perhaps the need for CORNEAL TRANSPLANTATION. Treatment seeks to relieve the irritation. In mild entropion, lubricating eye drops may be sufficient to protect the eye. Moderate to severe entropion requires surgery to restore the eyelid to its appropriate structure. Once corrected, entropion usually does not recur.

See also CORNEAL INJURY; ECTROPION; KERATITIS.

enucleation Surgical removal of a cancerous EYE or a severely diseased or damaged eye. The OPERATION, performed under general ANESTHESIA, takes about an hour. After removing the eye, the surgeon places an implant to fill the shape of the socket and provide a means of attaching a PROSTHETIC EYE. A pressure dressing stays in place over the eye orbit for one to two days to minimize swelling and allow the implant to become firmly rooted in the conjunctival tissue. During this time it is common as well as frightening for people to have difficulty opening the other eye, as the eyes are accustomed to functioning together. Once the bandage comes off and the eyelid of the operated eye is free to move, the eyelid for the unoperated eye resumes normal functioning. Complete HEALING takes about six weeks, during which time it is necessary to place anti-inflammatory and antibiotic drops in the operated eye socket to keep swelling and the risk for INFECTION to a minimum.

Though the operation is uncomplicated and the body quickly heals following the surgery, enucleation can be a difficult procedure for people to accommodate emotionally. Even when the eye has been visionless for a long time, the prospect of losing the eye troubles many people. The modern prosthetic eye is typically such a close match for the remaining eye that it is unapparent to other people. Once the operative site heals, the eye orbit (socket) and implant require little care or attention beyond cleaning the external eyelid area for hygienic purposes.

See also ANTIBIOTIC MEDICATIONS; RETINOBLASTOMA; SURGERY BENEFIT AND RISK MANAGEMENT; VISION IMPAIRMENT.

episcleritis INFLAMMATION of the episclera, the membrane that covers the sclera (fibrous outer layer, the "white," of the EYE). Most episcleritis is idiopathic (occurs for unknown reasons), though the condition sometimes accompanies AUTOIMMUNE DISORDERS such as RHEUMATOID ARTHRITIS and REITER'S SYNDROME. Episodes are self-limiting though may recur over time, with each episode of inflammation generally lasting 7 to 10 days. Symptoms may include mild irritation and redness, and occasionally a nodule (bump) on the surface of the sclera. The doctor can diagnose episcleritis by its appearance. Lubricating eye drops help relieve the irritation until the inflammation subsides. This is usually the only treatment necessary. Some studies suggest a correlation between episcleritis and hormonal shifts such as occur with the MENSTRUAL CYCLE or MENOPAUSE. Episcleritis is three times more common in women than men. Episcleritis does not affect vision or result in any long-term effects on the health of the eye.

See also CONJUNCTIVITIS; KERATITIS; SCLERITIS.

exophthalmos Bulging outward of the EYE, sometimes called poptosis. Most exophthalmos results from Graves's disease and is a classic symptom of this form of HYPERTHYROIDISM. Thyroid-related exophthalmos results from swelling of the tissues around the eye and within the orbit that develops in reaction to the high levels of thyroid HORMONE present in the circulation. Other causes of exophthalmos include ORBITAL CELLULITIS, the autoimmune disorder Wegener's granulomatosis, and FRACTURE of the facial or orbital bones that push the eye out of place. Less common causes of exophthalmos include tumors of the eye, OPTIC NERVE, or BRAIN that protrude into the orbital socket and ANEURYSM (ballooning of the arterial wall) of the internal carotid ARTERY, a branch of which runs behind the eye. Exophthalmos can affect one eye (unilateral) or both eyes (bilateral), and when bilateral can affect one eye more prominently than the other.

Exophthalmos can cause significant and permanent vision impairment, and requires prompt treatment.

The diagnostic path begins with an OPHTHALMOLOGIC EXAMINATION and blood tests to assess thyroid function. When Graves's disease or hyperthyroidism is the cause, treatment to restore appropriate levels of thyroid hormones often though not always returns the eye to its normal position. Persistent exophthalmos may prevent the eyelids from closing over the eye, exposing the CORNEA to excessive dryness and potential trauma. Untreated exophthalmos results in VISION IMPAIRMENT that can progress to blindness.

See also AUTOIMMUNE DISORDERS; GRAVES'S OPHTHALMOPATHY.

eye The organ of vision. The paired eyes work in coordination to present NERVE impulses the BRAIN interprets as dimensional (stereovisual) images. The function of sight requires close integration among the structures of the eye, the neurologic system, and the muscular system. Each eye is a fluid-filled, elongated globe of fibrous tissue, about ¼ inch from front to back and 1 inch from top to bottom and side to side, contained within the protective cavity of the orbital socket in the skull. The OPTIC NERVE, the second cranial nerve, provides a direct pathway from the back of the eye to the brain. Six muscles move each eye up and down, from side to side, and in rotation. These muscles direct the eye toward objects within the VISUAL FIELD and hold the eyes steady.

The process of vision begins when lightwaves enter the eye through the CORNEA, a transparent portion of the eye's tough outer layer, the sclera. The cornea's convex front surface initially refracts the lightwaves for preliminary focusing. The cornea is soft and flexible but fixed; it does not adjust or move. The LENS, a transparent and flexible convex disk behind the cornea, further refracts the lightwaves. Tiny muscles at the edge of the lens, the ciliary muscles, cause the lens to thicken or flatten to adjust the degree of refraction for optimal focus. The resulting light pattern strikes the RETINA, activating the specialized cells that detect color (cones) and brightness (rods). These cells convert the light to nerve impulses that converge at the back of the retina at the optic disk, their portal to the optic nerve. The optic nerve conveys the signals to the brain, which interprets them as images.

COMMON CONDITIONS OF THE EYE

AMBLYOPIA	ASTIGMATISM
BLEPHARITIS	CATARACT
CONJUNCTIVITIS	CORNEAL INJURY
DRY EYE SYNDROME	EYE STRAIN
FLOATERS	GLAUCOMA
HORDEOLUM	HYPEROPIA
ISCHEMIC OPTIC NEUROPATHY	KERATITIS
KERATOCONUS	MYOPIA
NIGHT BLINDNESS	PRESBYOPIA
RETINAL DETACHMENT	RETINITIS PIGMENTOSA
RETINOPATHY	STRABISMUS
VISION IMPAIRMENT	

For further discussion of the eye within the context of ophthalmologic structure and function please see the overview section "The Eyes."

See also AGING, VISION AND EYE CHANGES THAT OCCUR WITH; CRANIAL NERVES.

eye pain Sensations discomfort involving the EYE and its supporting structures. Eye PAIN may vary

COMMON CAUSES OF EYE PAIN

Quality of Pain	Possible Causes	Medical Attention Required
itchy or scratchy sensation	DRY EYE SYNDROME, ALLERGIC CONJUNCTIVITIS, dirty contact lenses, EYE STRAIN	self-care such as artificial tears or ANTIHISTAMINE MEDICATIONS; timely doctor's assessment if symptoms persist after self-care efforts to relieve them
burning and PHOTOPHOBIA, may include discharge	CONJUNCTIVITIS, HORDEOLUM, CHALAZION, BLEPHARITIS, KERATITIS, DACRYCYSTITIS, ENTROPION	prompt doctor's assessment; infections require antibiotic medications
burning, photophobia, excessive tearing, visible blisters on surface of the eye	BULBOUS KERATOPATHY, CICATRICIAL PEMPHIGOID, corneal abrasion	immediate medical attention
sharp, deep, or intense pain that may increase with, or prevent, eye movement	ORBITAL CELLULITIS, trauma to eye, GLAUCOMA, optic neuritis, chemical or flash BURNS	medical emergency

from scratchy irritation to intense and debilitating pain. Much eye pain in the form of burning and itching arises from minor and treatable causes that affect the structures around the eye rather than the eye itself. Eye pain that is throbbing, stabbing, deep, or accompanies visual disturbances may suggest conditions such as GLAUCOMA.

Eye pain that is sudden and severe, accompanies partial or complete loss of vision, prevents movement of the eye, or follows TRAUMA TO THE EYE or face requires emergency medical attention. When there is the possibility of penetrating eye injury, loosely patch both eyes to minimize movement.

The diagnostic path begins with careful examination of both eyes, which may include OPHTHALMOSCOPY, FLUORESCEIN STAINING when the doctor suspects CORNEAL INJURY, TONOMETRY to measure the pressure inside the eye, and SLIT LAMP EXAMINATION for further assessment of the RETINA and other structures of the inner eye. The doctor may place an anesthetic medication (numbing eye drops) in the eye to determine whether the pain is coming from the surface of the eye, in which case the pain will go away, or from within the eye, in which case the pain will persist. Often the doctor will also conduct basic tests of VISUAL ACUITY such as a SNELLEN CHART reading.

People who wear contact lenses should remove them at the first sign of discomfort. Treatment for eye pain targets the underlying cause. Most minor causes resolve without complications or permanent VISION IMPAIRMENT. Causes such as severe corneal injury (BURNS, lacerations), glaucoma, and ORBITAL CELLULITIS seriously threaten vision and can result in permanent and complete vision loss without urgent and appropriate treatment.

See also RETINAL DETACHMENT.

eye strain The sensation of tiredness and irritation of the eyes, often accompanying long periods of time involved in performing the same task such as reading, computer work, watching television, playing video games, and assembly work. EYE strain generally results from overuse of the muscles that move the eyes. The overuse tires the muscles, which become less responsive to the focusing needs of the eyes. The difficulty generates temporary vision disturbances such as blurring, and may also cause muscle tension headaches. Insufficient blinking, which causes the eyes to become dry and irritated, often accompanies the overuse.

These measures can help relieve eye strain:

- Blink frequently.
- Use artificial tears to improve the moisture content of the eyes.
- Make sure lighting is of the appropriate intensity and placement.
- Reduce glare and reflection.
- Look away from close tasks every 10 to 15 minutes to focus on objects in the distance.
- Wear reading glasses or CORRECTIVE LENSES to accommodate PRESBYOPIA.
- Wear eye protection when in environments that are dusty or windy, and when in the sun.

Contrary to popular belief, eye strain (such as reading in dim light) does not cause permanent VISION IMPAIRMENT. However, eye strain may result from undetected vision impairment, such as ASTIGMATISM and HYPEROPIA, that affect the eye's ability to focus on near objects. An ophthalmologist or optometrist should evaluate eye strain that persists despite efforts to improve the visual environment.

See also ERGONOMICS; HEADACHE; MUSCLE; OCCUPATIONAL HEALTH AND SAFETY; VISION HEALTH.

F

farsightedness See HYPEROPIA.

flashes Visual phantoms that appear as spots of light. An ophthalmologist should evaluate occurrences of flashes, as they can be symptoms of RETINAL DETACHMENT or other conditions affecting the RETINA. Flashes represent stimulation of the rods and cones, the cells of vision carpeting the retina, that occurs when the gelatinous fluid holding the retina in place (vitreous humor) moves across them. Because the NERVE signals these cells send to the BRAIN encode patterns of light, the brain interprets messages from them as light. A blow to the head that causes a person to "see stars" has similar effect when it is forceful enough to jostle the vitreous humor against the retina. Flashes may appear as multiple spots of light, "light showers," or lightning-like streaks.

The ophthalmologist typically performs a full OPHTHALMIC EXAMINATION to assess the integrity of the retina. Prompt treatment is necessary to intervene with a retinal tear or retinal detachment, to preserve vision. Isolated flashes of light generally are harmless and may occur for various reasons. Lines or waves of light that last 20 to 60 minutes are common with migraine headaches and have no significance for vision or the health of the eye.

See also FLOATERS; HEADACHE; VISION IMPAIRMENT; VITREOUS DETACHMENT.

floaters Fragments of inner EYE material that float through the vitreous humor, casting shadows against the RETINA as entering light strikes them. Floaters may take various shapes and sizes, and typically move around the VISUAL FIELD, changing position with blinking or eye movement. Most floaters are harmless, though large floaters may interfere with vision. Holding the eye still may allow the floater to settle to the bottom of the eye, out of the visual field. A sudden increase in the number of floaters, or floaters that occur in combination with FLASHES, can signal a retinal tear or RETINAL DETACHMENT. Prompt intervention is necessary to prevent further retinal damage and preserve vision. Floaters may also indicate UVEITIS. Large floaters may remain indefinitely; small floaters may eventually break apart and become absorbed into the vitreous humor. There is no treatment for floaters.

See also VISION IMPAIRMENT; VITREOUS DETACHMENT.

fluorescein staining A simple procedure for diagnosing CORNEAL INJURY or foreign objects in the EYE. The ophthalmologist places a strip of paper containing fluorescein at the edge of the eye. The dye rapidly leaches into the tears. Some people experience a slight burning sensation when the dye washes across the eye for the first time. Blinking disperses the tears across the CORNEA. With the regular room lights turned off, the ophthalmologist shines a cobalt blue light on the eye. Any breach in the eye's surface shows as bright green. The tears wash the fluorescein from the eye within a few minutes.

See also OPHTHALMIC EXAMINATION; SLIT LAMP EXAMINATION; TRAUMA TO THE EYE.

G

glaucoma A serious and progressive EYE condition in which the cells at the front of the OPTIC NERVE where it intersects with the RETINA, the retinal ganglia, die, resulting in vision loss. Early diagnosis and treatment can minimize vision loss. Health experts estimate that 5 million Americans have glaucoma, though only about 2 million of them know it. Glaucoma is the third-leading cause of blindness in the United States, primarily because it remains undetected until damage to the optic NERVE becomes significant. Glaucoma becomes more common after age 65, though there is a congenital form that manifests in early childhood (congenital glaucoma).

Until the late 1990s ophthalmologists perceived glaucoma to be the exclusive consequence of increased pressure within the eye (INTRAOCULAR PRESSURE) that caused the death of retinal ganglia cells. Current understanding of the disease process of glaucoma affirms the death of retinal ganglia cells as the cause of damage to the optic nerve, though recognizes that numerous factors, intraocular pressure being only one among them, contribute to this damage. About 30 percent of people who have glaucoma have normal intraocular pressure, and only about 10 percent of people who have elevated intraocular pressure have glaucoma.

There are two general forms of glaucoma: open angle and closed angle (also called angle-closure). The designations refer to whether the channel through which aqueous humor drains from the eye, called the angle, is open but dysfunctional (open-angle glaucoma) or becomes blocked by the iris (closed-angle glaucoma). In glaucoma, the drainage angle either malfunctions (open-angle glaucoma) or a segment of the iris seals over it (closed-angle glaucoma). When the aqueous humor cannot properly drain, it causes the pressure to increase in the anterior chamber. Increased pressure in the chambers puts increased pressure on the inner eye, causing intraocular pressure to rise. Extreme or extended elevations in intraocular pressure compress the optic disk, causing nerve cells to die.

Acute closed-angle glaucoma requires emergency medical attention. Without immediate treatment, severe to complete vision loss can occur within hours of the onset of symptoms.

Open-angle glaucoma is chronic, progressing over years, and is the most common form of glaucoma, accounting for about 85 percent. Closed-angle glaucoma can be acute, with the sudden onset of severe symptoms, or chronic with symptoms similar to those of open-angle glaucoma. The function and dysfunction of aqueous humor drainage is the dimension of glaucoma doctors and researchers understand most clearly, and most treatment approaches target reducing aqueous humor production or improving its drainage from the eye. Less clear are the other factors that contribute to death of the retinal ganglia cells and corresponding destruction of the optic disk. These factors are especially significant for the 30 percent of people who have glaucoma with normal intraocular pressure. Researchers are investigating the roles of genetics, autoimmune processes, and correlations with conditions such as DIABETES and HYPERTENSION (high BLOOD PRESSURE).

Symptoms and Diagnostic Path

The key symptom of chronic glaucoma, open-angle or closed-angle, is the gradual and painless loss of VISUAL ACUITY and VISUAL FIELD. Often the

pattern of progression begins with loss of peripheral (outside) vision. Over time the field of vision becomes increasingly narrow, which people often describe as "tunnel vision." Other symptoms include excessive tearing (especially with close focus tasks such as reading), halos around lights at night, aching eyes, and headaches. Sudden throbbing PAIN in the eye, loss of vision, severe HEADACHE, halos around lights, and a dilated pupil in the affected eye are symptoms of acute closed-angle glaucoma.

GLAUCOMA SYMPTOMS

Chronic (Open-Angle or Closed-Angle)	Acute Closed-Angle
slow loss of peripheral vision	sudden, throbbing PAIN in the EYE
"blind spots" in the field of vision	sudden, severe HEADACHE
halos around lights at night	sudden restriction or loss of vision
teary eyes with close focus tasks	dilated pupil in affected eye
achiness in the affected eye	NAUSEA and vomiting

Though eye care practitioners routinely use TONOMETRY to screen for increased intraocular pressure, this test alone is not sufficient to detect glaucoma. Detecting glaucoma requires a full OPHTHALMIC EXAMINATION including fundus examination to assess the condition of the optic disk. The ophthalmologist will also conduct a visual acuity test and a peripheral vision test. Other procedures that can help diagnose glaucoma in its early stages or quantify the extent of damage in moderate to advanced glaucoma are ULTRASOUND of the eye and OPTICAL COHERENCE TOMOGRAPHY (OCT).

Treatment Options and Outlook

Acute closed-angle requires emergency measures to relieve intraocular fluid and the accumulation of aqueous humor. Such measures typically include a combination of procedures to open the drainage angle, ophthalmic medications to lower intraocular pressure, and systemic medications to draw fluid from cells (osmotics). The ophthalmologist is also likely to administer medications for pain and to minimize NAUSEA and vomiting. Ongoing treatment with glaucoma medications or glaucoma surgery is then necessary. Ophthalmic medications (drops, inserts, and ointments) to open the drainage angle and lower intraocular pressure are the standards of treatment for chronic glaucoma of either form, and typically can control glaucoma for many years.

Surgery becomes an option to treat glaucoma that becomes advanced or does not respond to

COMMON GLAUCOMA MEDICATIONS

Type of Drug	Actions
alpha-blockers (apraclonidine, brimonidine)—topical ophthalmic preparations	reduce aqueous humor production by slowing function of ciliary processes; increase drainage of aqueous humor
beta-blockers (betaxolol, carteolol, levobunolol, metipranolol, timolol)—topical ophthalmic preparations; oral products sometimes used	reduce aqueous humor production by slowing function of the ciliary processes
carbonic anhydrase inhibitors (brinzolamide, dorzolamide)—topical ophthalmic preparations	reduce aqueous humor production by blocking the action of the enzyme necessary for its production, carbonic anhydrase
miotics (pilocarpine, carbachol)—topical ophthalmic preparations	increase drainage of aqueous humor
prostaglandin analogs (latanoprost, travoprost, bimatoprost, unoprostone)—topical ophthalmic preparations	increase drainage of aqueous humor via secondary routes

medication therapy. Surgical treatments for glaucoma include the following:

- For iridotomy, the ophthalmologist uses an ophthalmologic laser to place a small opening in the iris. The opening provides another route of drainage for the aqueous humor and helps keep the iris from blocking the drainage angle in open-angle glaucoma.
- For trabeculoplasty, the ophthalmologist uses an ophthalmologic laser to make numerous "dots" in the trabecular meshwork—the fanlike network of tiny channels at the end of the angle that disperse the draining aqueous humor—to expand its the draining capacity.
- For trabeculotomy, the ophthalmologist places an aqueous shunt, a tiny opening from the anterior chamber through the sclera, to allow aqueous humor to drain to the outside of the eye.
- For cytophotocoagulation, the ophthalmologist uses an ophthalmologic laser to destroy portions of the ciliary processes to reduce aqueous humor production.

Early diagnosis and treatment offer the best opportunity for minimizing vision loss. It is important to diligently follow the directions for using glaucoma medications, as glaucoma requires consistent control. Appropriate treatment can slow the progression of vision loss in most people who have glaucoma.

Risk Factors and Preventive Measures

Age is the most significant risk factor for glaucoma; glaucoma is uncommon in people under age 40 and about two thirds of people who develop glaucoma are over age 65. Glaucoma is more common in people of African American and Asian ethnicity and tends to run in families. Glaucoma also is more likely to develop in people who have hypertension, ATHEROSCLEROSIS, diabetes, and severe MYOPIA (nearsightedness) and in people who take CORTICOSTEROID MEDICATIONS. Prevention focuses on regular ophthalmic examinations to detect glaucoma early in its course.

See also AGE-RELATED MACULAR DEGENERATION (ARMD); CATARACT; LASER SURGERY; VISION HEALTH.

Graves's ophthalmopathy Changes in the EYE that occur as a result of Graves's disease, a form of HYPERTHYROIDISM, and occasionally as a result of other forms of thyroid disease. The most prominent feature of Graves's ophthalmopathy is EXOPHTHALMOS, an outward bulging or protrusion of the eyes that often is the first indication of Graves's disease. The exophthalmos results from enlarged extraocular muscles (the muscles that move the eye) and edema (swelling due to retained fluid) in the tissues around the eye and within the ocular orbit (eye socket). This circumstance restricts the ability to move the eyes, particularly upward and side to side, as well as to close the eyelids. Graves's ophthalmopathy can involve only one eye (unilateral) though most often involves both eyes (bilateral). Symptoms and consequences range from mild to severe, with about 5 percent of people experiencing substantial loss of vision that may include loss of the eye. Graves's ophthalmopathy can appear before there are any indications of Graves's disease, at the onset of hyperthyroid symptoms, or months to years after the diagnosis of Graves's disease.

Graves's ophthalmopathy presents a significant threat to vision. The swelling in and around the orbit pressures the structures of the eye and can compress the OPTIC NERVE, which can result in OPTIC NERVE ATROPHY (the death of cells in the optic NERVE) and permanent VISION IMPAIRMENT. The external pressure against the eye also raises the pressure inside the eye (INTRAOCULAR PRESSURE), which can result in GLAUCOMA. The combination of exophthalmos and restricted lid movement prevents the eyelids from closing completely, which allows the CORNEA to become dry. The resulting irritation and INFLAMMATION (KERATITIS) reduces VISUAL ACUITY and also exposes the inner eye to INFECTION. Though the symptoms that threaten vision eventually subside, many of the changes that result, including exophthalmos and vision impairment, are permanent.

Symptoms and Diagnostic Path

The symptoms of Graves's ophthalmopathy include

- exophthalmos (sometimes called poptosis)
- DIPLOPIA (double vision)

- CONJUNCTIVITIS (inflammation of the inner eyelids)
- diminished visual acuity (blurry or distorted vision)
- PHOTOPHOBIA (sensitivity to light)
- excessive tearing

As these symptoms are distinctive for Graves's ophthalmopathy, the doctor often can make the diagnosis based on their presentation. Tests of thyroid HORMONE levels in the BLOOD confirm Graves's disease, if not already diagnosed. Conventional OPHTHALMIC EXAMINATION and SLIT LAMP EXAMINATION allow the ophthalmologist to assess the status of vision and health of the structures of the eye. A COMPUTED TOMOGRAPHY (CT) SCAN helps assess the extent of orbital swelling and compression of the optic nerve.

Treatment Options and Outlook

The course of Graves's ophthalmopathy seems to unfold in two stages, regardless of treatment for or status of the underlying hyperthyroidism. The first stage is the acute or active phase, during which symptoms emerge. During this stage, which extends over 18 to 30 months, ophthalmologic treatment focuses on reducing pressure on the eye and stabilizing vision, and may include

- ophthalmic lubricating drops or ointment to keep the cornea hydrated
- patching the eyes at night to protect the corneas during sleep
- NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to reduce inflammation and relieve discomfort
- CORTICOSTEROID MEDICATIONS to suppress the body's immune response
- ANTIBIOTIC MEDICATIONS to treat bacterial infection of the eyelids (BLEPHARITIS), conjunctiva (conjunctivitis), and cornea (keratitis)

In the second stage of Graves's ophthalmopathy, the progression of symptoms ends. However, the changes that have occurred are permanent. Fibrous deposits replace lymphocytes in the eye muscles, maintaining their enlargement and continuing the exophthalmos. Treatment in this stage targets minimizing these permanent consequences through surgeries to relieve the pressure within the orbit (orbital decompression), reduce the size of the extraocular muscles (myectomy), and reconstruct the eyelids so they close completely over the eye (BLEPHAROPLASTY). Corneal reshaping (keratoplasty) or CORNEAL TRANSPLANTATION may be necessary to restore vision when damage to the cornea is extensive. If infection resulted in loss of the eye, the ophthalmologist will place a PROSTHETIC EYE.

Risk Factors and Preventive Measures

Graves's ophthalmopathy occurs only in conjunction with thyroid disorders, nearly always hyperthyroidism. It may appear months to several years before other clinical indications of hyperthyroidism, or a comparable time after beginning treatment for hyperthyroidism. Prompt diagnosis and treatment are essential to preserve vision, as the changes that occur with Graves's ophthalmopathy are generally permanent. An ophthalmologist should evaluate any changes in the appearance of the eyes. Regular eye examinations help screen for Graves's ophthalmopathy as well as other eye health problems.

See also AUTOIMMUNE DISORDERS; BACTERIA; VISION HEALTH.

H

hordeolum A bacterial INFECTION of a gland or an eyelash follicle along the edge of the eyelid, commonly known as a stye. A hordeolum causes swelling, redness, PAIN, and a discharge that leaves a crusty layer on the eyelids during sleep. The doctor can usually diagnose hordeolum by its presentation. BLEPHARITIS (infection of the inside surface of the eyelid) and CONJUNCTIVITIS (infection of the conjunctiva, the membrane lining the eyelids) may instigate, accompany, or follow hordeolum. The doctor often chooses to anesthetize the area and lance (make tiny punctures or incisions under sterile conditions) the hordeolum to drain its contents and relieve the pressure. Further treatment is ophthalmic ANTIBIOTIC MEDICATIONS, typically in ointment form, applied to the area. Sometimes oral antibiotic medications are also necessary. Warm, moist compresses soothe the irritated tissues and help draw out any remaining pus.

Most hordeola clear up in 7 to 10 days with treatment and heal without residual consequences. A hordeolum does not itself cause VISION IMPAIRMENT, though untreated hordeola can lead to significant EYE problems if the infection spreads to other structures of the eye. Some people experience recurring hordeola, while others experience only a single episode. A hordeolum may also form the basis for a CHALAZION (painless nodule) to develop in its place.

See also BACTERIA; ECTROPION; ENTROPION.

hyperopia A refractive error, commonly called farsightedness, in which the EYE has difficulty focusing on near objects. Hyperopia results when the focal point of lightwaves entering the eye extends past the RETINA, causing the images the retina registers to be blurred. The refractive error occurs because the distance from the front to the back of the eye is shorter than normal. Symptoms of hyperopia include

- squinting when reading or doing close work
- HEADACHE
- fatigued eye muscles (aching around the eyes)
- blurred vision when looking at near objects yet clear vision when looking at distant objects

CORRECTIVE LENSES (eyeglasses or contact lenses) can compensate for hyperopia by altering the focal point of lightwaves so it falls directly on the retina. They do so by refracting (bending) the lightwaves outward. REFRACTIVE SURGERY, which permanently alters the shape of the CORNEA, can provide refractive correction for people with mild to moderate hyperopia. Hyperopia sometimes occurs following refractive surgery for MYOPIA (nearsightedness) as a consequence of overcorrection. Eye professionals denote refractive corrections in units of measure called diopters. For hyperopia, the expression of diopter is a positive number. Corrective lenses for hyperopia have a magnifying appearance that make the eyes look bigger than they are.

Hyperopia is less common than myopia, affecting about 20 to 25 percent of adults. Few people who have hyperopia have greater than +6 diopters of refractive error, so nearly always corrective measures result in normal VISUAL ACUITY.

See also ASTIGMATISM; PRESBYOPIA; REFRACTIVE ERRORS.

I

intraocular pressure The pressure within the EYE that maintains the eye's form and structure. Normal intraocular pressure in an adult is 12 to 22 millimeters of mercury (mm Hg). A device called a tonometer measures intraocular pressure, either through light contact against the anesthetized eye or via the force of resistance to a puff of air blown against the eye's surface (a noncontact method that does not require anesthetic drops). Elevated intraocular pressure is called ocular hypertension. Lower than normal intraocular pressure is called ocular hypotension.

Ocular hypertension (greater than 21 mm Hg) is a hallmark sign of GLAUCOMA, an eye condition that, if untreated, results in complete loss of vision. Other health conditions that can increase intraocular pressure include tumors that press against the eye, ORBITAL CELLULITIS, and GRAVES'S OPHTHALMOPATHY. Increased intraocular pressure damages the cells on the front of the OPTIC NERVE (the retinal ganglia), leading to permanent VISION IMPAIRMENT. Ophthalmic medications that reduce intraocular pressure work through various mechanisms, depending on the cause of the increased pressure.

Ocular hypotension, in which the intraocular pressure is lower than normal (less than 12 mm Hg), characterizes chronic UVEITIS (INFLAMMATION of the structures of the eye) and of certain tumors of the eye. Ocular hypotension also sometimes accompanies systemic HYPOTENSION (low BLOOD PRESSURE) and as a SIDE EFFECT of medications, notably general anesthesia agents.

See also OPHTHALMIC EXAMINATION; TONOMETRY; VITRECTOMY; VITREOUS DETACHMENT.

iritis INFLAMMATION of the iris, the MUSCLE surrounding the pupil of the EYE. Iritis may develop as a result of INFECTION, such as CONJUNCTIVITIS that spreads to involve other structures of the eye. Iritis also occurs as part of the inflammatory process in AUTOIMMUNE DISORDERS such as RHEUMATOID ARTHRITIS. The symptoms of iritis include

- irritation and a "gritty" sensation in the eye
- redness of the eye
- PHOTOPHOBIA (sensitivity to bright light)
- blurry vision
- excessive tearing

The ophthalmologist can diagnose iritis based on the appearance of the iris and the eye, though will additionally perform a SLIT LAMP EXAMINATION to look for involvement of other structures of the eye. Treatment is ophthalmic ANTIBIOTIC MEDICATIONS (eye drops or ointment) when the ophthalmologist suspects bacterial infection and ophthalmic CORTICOSTEROID MEDICATIONS to reduce the inflammation. When the cause of the inflammation is systemic, the ophthalmologist may prescribe anti-inflammatory medications such as corticosteroids or NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). Treatment usually resolves the symptoms without residual VISION IMPAIRMENT. Untreated or recurrent iritis can have long-lasting effects on vision, including increased INTRAOCULAR PRESSURE.

See also BACTERIA; EPISCLERITIS; GLAUCOMA; KERATITIS; SCLERITIS; UVEITIS.

ischemic optic neuropathy Damage to the OPTIC NERVE resulting from insufficient blood supply, sometimes called "STROKE" of the optic nerve. Ischemic optic neuropathy is occurs most commonly in people over age 55 and causes mild to

complete VISION IMPAIRMENT. There are two forms: arteritic, associated with giant-cell arteritis (an inflammatory disorder of the arteries that typically affects the temporal arteries) and nonarteritic, which correlates with CARDIOVASCULAR DISEASE (CVD) such as HYPERTENSION (high BLOOD PRESSURE) and ATHEROSCLEROSIS. Other conditions associated with the nonarteritic form include DIABETES, HYPOTENSION (low blood pressure), and RHEUMATOID ARTHRITIS.

Vision impairment due to ischemic optic neuropathy comes on suddenly. In a characteristic pattern, a person wakes up in the morning with noticeable loss of VISUAL ACUITY and VISUAL FIELD. This may continue for several days, improving as the day goes on, though in short order becomes permanent. The diagnostic path begins with OPHTHALMOSCOPY and SLIT LAMP EXAMINATION to visualize the optic disk (portion of the optic nerve that attaches to the RETINA), which appears pale and swollen. Diagnosis of giant cell arteritis by temporal ARTERY biopsy confirms the diagnosis of the arteritic form of ischemic optic neuropathy. Doctors arrive at the diagnosis of the nonarteritic form on the basis of symptoms and ruling out other causes.

Treatment for arteritic ischemic optic neuropathy is CORTICOSTEROID MEDICATIONS to reduce the INFLAMMATION. Vision loss, however, is irreversible. There are no effective treatments for the nonarteritic form, which does not appear to improve with corticosteroids. Lifestyle modifications such as SMOKING CESSATION improve circulation in general with the presumption that such improvement also affects optic structures. ASPIRIN THERAPY, such as prescribed as a prophylactic measure for HEART ATTACK and stroke, may have a preventive effect with the arteritic form. It is especially important to manage underlying health conditions that affect circulation, such as hypertension and diabetes.

When the ischemic optic neuropathy affects only one EYE, the person can make adaptations and adjustments to accommodate the vision impairment that do not necessarily require substantial changes in lifestyle. Most people can still read, work, and perform other functions of daily living with visual acuity in only one eye. Ischemic optic neuropathy that involves both eyes can significantly affect lifestyle.

See also TOXIC OPTIC NEUROPATHY; VASCULITIS.

K

keratitis INFLAMMATION of the CORNEA, usually the result of an INFECTION. The cause of the infection is more commonly viral, such as HERPES SIMPLEX or HERPES ZOSTER, than bacterial. Symptoms of infectious keratitis include

- redness and irritation of the EYE and conjunctiva (inner eyelids)
- discomfort or PAIN
- excessive tearing
- difficulty keeping the eye open
- diminished VISUAL ACUITY (usually blurred vision)
- eye discharge or crusting

Viral keratitis usually runs its course without complication, though occasionally a secondary bacterial infection may develop. ANTIVIRAL MEDICATIONS sometimes shorten the course of chronic herpes infections. Bacterial keratitis typically follows a CORNEAL INJURY, such as an abrasion or laceration, and requires treatment with ophthalmic ANTIBIOTIC MEDICATIONS. Chronic or recurrent keratitis can cause permanent scarring of the cornea, resulting in diminished visual acuity such as ASTIGMATISM. Extensive corneal damage may require CORNEAL TRANSPLANTATION.

SUNBURN is the most common cause of noninfectious keratitis. Extended exposure to the sun, especially on or around water, exposes the surface of the eye to the same ultraviolet rays that cause sunburn of the SKIN. Ultraviolet burns to the cornea are painful; treatment with ophthalmic CORTICOSTEROID MEDICATIONS helps reduce the inflammation.

See also BACTERIA; CONJUNCTIVITIS; EPISCLERITIS; IRITIS; SCLERITIS; SUN PROTECTION; UVEITIS; VIRUS.

keratoconus A degenerative disorder in which the CORNEA thins, allowing it to protrude from the surface of the EYE in somewhat of a cone shape. Keratoconus affects both eyes though often progresses at different rates in each eye. Ophthalmologists do not know what causes keratoconus, though it appears to run in families. Keratoconus is painless though results in progressive VISION IMPAIRMENT, typically in the forms of MYOPIA (nearsightedness) and ASTIGMATISM (distortions of vision resulting from the irregular surface of the cornea). As these REFRACTIVE ERRORS are the primary symptoms, the keratoconus may not become apparent until the coning becomes obvious.

Treatment for mild to moderate keratoconus is rigid gas-permeable contact lenses, which correct the refractive errors of vision as well as help contain the shape of the cornea. As the keratoconus progresses, however, contact lenses become less effective, and the thinned cornea may not be able to tolerate them. Keratoconus ultimately destroys the cornea and is a leading reason for CORNEAL TRANSPLANTATION, which replaces the diseased cornea with a donor cornea. Corneal transplantation successfully restores vision in about 90 percent of people who have keratoconus and undergo the procedure.

In 2004 the US Food and Drug Administration (FDA) approved a new treatment for keratoconus, corneal inserts, which are tiny plastic rings the ophthalmologist implants along the edge of the cornea. The corneal inserts flatten the cornea, reducing the coning. Corneal inserts come in different thicknesses to allow less or more flattening and are replaceable.

See also CORNEAL INJURY; CORRECTIVE LENSES.

L–M

lens The primary focusing structure of the EYE, located in the center at the front of the eye. The lens is transparent, convex (rounded outward on each side), round, and flexible. A thin membrane encloses the lens. Tiny muscles at the front edges of its sides, the ciliary muscles, contract to flatten the lens and relax to thicken the lens. These adjustments alter light refraction (the angle at which the lens bends lightwaves entering the eye) to accommodate near and distant vision. The most common health conditions that affect the lens are PRESBYOPIA, in which the FLEXIBILITY of the lens diminishes with aging, and CATARACT, in which protein deposits cloud the lens and obscure vision. The lens is also vulnerable to accidental injury, particularly from blunt force (such as a baseball) or puncture.

For further discussion of the lens within the context of ophthalmologic structure and function please see the overview section "The Eyes."

See also CATARACT EXTRACTION AND LENS REPLACEMENT; CORNEA; HYPEROPIA; MYOPIA; REFRACTIVE ERRORS; RETINA; VISION IMPAIRMENT.

mydriasis Excessive or persistent dilation of the pupil that is a symptom of ophthalmic or systemic conditions. The ophthalmologist may induce mydriasis, using topical atropine, to examine the inner EYE. Therapeutic mydriasis using atropine-based ophthalmic drops is an alternate treatment for AMBLYOPIA. Two eye conditions can cause mydriasis: GLAUCOMA and damage to the iris. In the healthy eye the iris, a muscular membrane, controls the opening of the pupil. INFLAMMATION of or tears in the iris affect its ability to function, which also can result in mydriasis.

Other causes of mydriasis are systemic, involving damage to NERVOUS SYSTEM structures and functions, and may include TRAUMATIC BRAIN INJURY (TBI), STROKE, and medication response such as with narcotic use, which causes the muscles to relax. Eye disorders often affect only one eye (unilateral mydriasis), whereas systemic conditions typically affect both eyes (bilateral mydriasis). PHOTOPHOBIA (sensitivity to bright light) often accompanies mydriasis as the dilated pupil cannot limit light from entering the eye. VISION IMPAIRMENT depends on the extend of the dilation; a fully dilated pupil prevents focus on near objects.

The diagnostic path begins with a basic OPHTHALMIC EXAMINATION including SLIT LAMP EXAMINATION and OPHTHALMOSCOPY, unless there is clear evidence that the mydriasis results from systemic causes. TONOMETRY, which measures the pressure within the eye (INTRAOCULAR PRESSURE), determines whether glaucoma is present. Tears of the iris are typically apparent when looking at the eye as they distort the iris (the colored portion of the eye). Inflammation of the iris (IRITIS) often reddens the eye and is apparent with ophthalmoscopy. Further diagnostic measures turn to NEUROLOGIC EXAMINATION. Treatment targets the causative condition.

See also EYE PAIN; NARCOTICS; TRAUMA TO THE EYE.

myopia A refractive error commonly called nearsightedness, in which the EYE has difficulty focusing on distant objects. Myopia results when the focal point of lightwaves entering the eye falls short of the RETINA, causing the images the retina registers to be blurred. The refractive error occurs because the distance from the front to the back of the eye is longer than normal. Symptoms of myopia include

- squinting when looking at distant objects
- straining to see when driving

- difficulty seeing the ball when playing baseball, tennis, and similar sports
- frequent headaches at the end of the day

CORRECTIVE LENSES (eyeglasses or contact lenses) can compensate for myopia by altering the focal point of lightwaves so it falls directly on the retina. They do so by refracting, or bending, the lightwaves inward. Eye professionals denote refractive corrections in units of measure called diopters. For myopia, the expression of diopter is a negative number. REFRACTIVE SURGERY, which permanently alters the shape of the CORNEA, provides refractive correction for mild to moderate myopia (–1 to –15 diopters). In 2004 the US Food and Drug Administration (FDA) approved an implantable contact lens to improve severe myopia (–15 to –30 diopters). Severe myopia sometimes cannot be fully corrected, resulting in VISION IMPAIRMENT with functional limitations or legal blindness. Myopia is the most common refractive error, affecting about 35 percent of adults.

See also ASTIGMATISM; HYPEROPIA; PRESBYOPIA; REFRACTIVE ERRORS.

N

nearsightedness See MYOPIA.

night blindness Impaired dark adaptation resulting from slowed photochemical reactions in the rods, the specialized cells of the RETINA that perceive contrast and detect visual images in low light. Night blindness becomes increasingly common after middle age. The person with night blindness may be unable to see at all in dim light or may experience delayed adjustment when going from a lighted environment to a dim or dark environment. A diminished VISUAL FIELD with restricted peripheral vision also contributes to night blindness, as the outer edge of the retina where peripheral vision takes place contains mostly rods.

There are not many treatment options for night blindness. Nutritional supplementation of vitamin A and the antioxidants LUTEIN and ZEAXANTHIN, which some studies show help maintain the health of the eye and improve the functioning of the rods, seem to aid some people. Adequate lighting when reading and especially when watching television or movies reduces the need for the eye to make accommodations for changing light. Increased lighting can compensate for diminished dark adaptation in static settings such as rooms and offices, though it is not possible to make similar accommodations for functions such as driving.

See also AGING, EYE AND VISION CHANGES THAT OCCUR WITH; ANTIOXIDANT; PRESBYOPIA; VISION HEALTH.

nystagmus Involuntary movements of the eyes, usually rapid and repetitive. Nystagmus can be congenital or acquired; in either circumstance it is a symptom of underlying disorders rather than itself a condition. Nystagmus nearly always indicates VISION IMPAIRMENT; if congenital, the impairment may improve or completely resolve with age. Vision impairment in adults depends on the underlying cause of the nystagmus. Temporary induced nystagmus, such as may occur with caloric testing (warm or cool water infused into the auditory canal) to assess disorders of the vestibular system, does not affect vision, although vestibular disorders can cause nystagmus.

Causes of Congenital Nystagmus	Causes of Acquired Nystagmus
ALBINISM (absence of retinal pigmentation)	vestibular disorders
congenital macular defects	brainstem or cerebellum damage or tumor
congenital CATARACT	MULTIPLE SCLEROSIS
absence of iris	TRAUMATIC BRAIN INJURY(TBI)
anomalies of the OPTIC NERVE	TRAUMATIC BRAIN INJURY(TBI)
	chronic ALCOHOL abuse

The diagnostic path includes a comprehensive OPHTHALMIC EXAMINATION and NEUROLOGIC EXAMINATION. Treatment targets the underlying cause. Some adults who have acquired nystagmus receive relief from the muscle relaxant medication baclofen (Lioresal), which interrupts NERVE signals from the BRAIN to the muscles that control the eyes. The long-term consequences for vision depend on the cause and duration of the nystagmus. Occasionally nystagmus occurs as an undesired SIDE EFFECT of antiseizure medications, and typically goes away with switching to another medication.

See also BENIGN PAROXYSMAL POSITIONAL VERTIGO (BPPV); DIPLOPIA; MUSCLE RELAXANT MEDICATIONS; PHOTOPHOBIA; STRABISMUS.

ocular herpes simplex An INFECTION of the eyes with HERPES SIMPLEX VIRUS 1 (HSV-1), which causes cold sores, or herpes simplex virus 2 (HSV-2), which causes GENITAL HERPES. The virus spreads to the eye to cause the initial infection via contamination from contact with an existing herpes sore elsewhere on the body. Ocular herpes simplex features similar eruptions of sores on the surface of the EYE and inside the eyelids. The sores are very painful and can cause permanent scarring of the CORNEA.

About half of people who have one outbreak of ocular herpes simplex will experience a second; about 20 percent have persistently recurring infections, ranking ocular herpes simplex as the leading infectious cause of corneal destruction. A serious complication of ocular herpes simplex is stromal KERATITIS, in which the IMMUNE SYSTEM begins to attack the stromal cells that make up the cornea. This leads to scarring deep within the cornea, resulting in distortions of vision and diminished VISUAL ACUITY.

The sores of ocular herpes simplex are characteristic of the infection. The antiviral medication acyclovir may reduce the severity of outbreaks of the infection when taken at the first sign of symptoms. Some studies show that taking acyclovir for 12 months significantly reduces recurrent ocular herpes simplex. However, there is no cure for herpes infection. Damage that occurs as a consequence of infection is permanent. Infection-control methods, such as frequent HAND WASHING and keeping the fingers away from the eyes, can help prevent initial infection.

See also ANTIVIRAL MEDICATIONS; AUTOIMMUNE DISORDERS; COLD SORE; CORNEAL INJURY; CORNEAL TRANSPLANTATION.

ocular herpes zoster INFECTION of the eyes with the varicella zoster VIRUS, a member of the HERPES SIMPLEX family of viruses that causes CHICKENPOX and shingles. After the infectious stage of chickenpox subsides, the virus submerges itself in NERVE roots. It may reemerge years to decades later, erupting in a rash of painful blisters along a nerve tract that hosts the virus. Ocular herpes zoster occurs when an outbreak that affects the face, usually along the tract of the trigeminal nerve, spreads to the EYE. Usually the outbreak affects only the eye on the same side of the face as the shingles eruption, though sometimes the shingles eruption affects both sides of the face. When this is the case, ocular herpes zoster can affect both eyes as well. As in other locations, the shingles blisters in the eye cause intense PAIN.

The blisters and pain are characteristic of ocular herpes zoster, making it possible for the doctor to make the diagnosis based on their presentation. Treatment typically includes ANTIVIRAL MEDICATIONS (such as acyclovir), ophthalmic CORTICOSTEROID MEDICATIONS to reduce INFLAMMATION, tricyclic ANTIDEPRESSANT MEDICATIONS to prevent postherpetic NEURALGIA, and ANALGESIC MEDICATIONS to relieve pain. Symptoms may take several weeks to several months to resolve. Numerous complications are possible that can have long-term consequences for vision, including GLAUCOMA and CATARACT. Ocular herpes zoster very seldom recurs, though this is a risk for those who are immunocompromised such as with HIV/AIDS or receiving IMMUNOSUPPRESSIVE THERAPY such as following ORGAN TRANSPLANTATION.

See also BLISTER; CORNEAL TRANSPLANTATION.

ophthalmic examination The basic diagnostic procedures an ophthalmologist uses to assess the

health of the EYE and vision, and detect problems with the structures and functions of the eye. The standard ophthalmic examination includes several components. For certain parts of the examination the ophthalmologist may place drops in the eyes that anesthetize the eye and dilate the pupils, to facilitate examining the structures of the back of the eye such as the RETINA and optic disk. Some people experience mild stinging when the drops first enter the eye. There is otherwise no discomfort with an ophthalmic examination. The complete exam takes about 10 minutes.

Physical Examination

The ophthalmologist begins with an examination of the orbital tissues, outer eyelids, inner eyelids, and conjunctiva (membrane lining the inner eyelids) of first one eye and then the other, checking to see that the eyelids open and close properly and looking for any growths or irritation. The ophthalmologist then checks the movement of the eyes, typically by asking the person to follow the track of an object such as a pen. Using a small light, the ophthalmologist checks the reaction of the pupils. These procedures help the ophthalmologist to assess the basic neurologic aspects of the eye's functions.

Visual Acuity and Visual Field

The familiar SNELLEN CHART test for VISUAL ACUITY features lines of letters in differing sizes and order of presentation. Covering first one eye and then the other, the person reads the line with the smallest letters that appear clear. The ophthalmologist records the result as a ratio that represents actual visual acuity compared to a standard of 20/20, with a score of 20/20 being what the normal eye sees at a distance of 20 feet. Diminished visual acuity may result from REFRACTIVE ERRORS such as MYOPIA (nearsightedness) or HYPEROPIA (farsightedness), or signal conditions of the eye such as CATARACT or GLAUCOMA.

The ophthalmologist tests for basic VISUAL FIELD by having the person focus on an object in the distance and signal when he or she can see an object (such as a pen the ophthalmologist holds) that moves into the field of normal vision. This test assesses peripheral vision and helps detect scotomas (small blind spots in the field of vision), which are both symptoms of glaucoma and RETINITIS PIGMENTOSA.

Slit Lamp Examination

The SLIT LAMP EXAMINATION, also called a biomicroscopic examination, uses light focused as an elongated slit in combination with magnification. Slit lamp examination allows the ophthalmologist to closely examine the front structures of the eye including the sclera, CORNEA, iris, and LENS. It is a common procedure for diagnosing cataract. The ophthalmologist may also use FLUORESCEIN STAINING to check for CORNEAL INJURY such as ABRASIONS or lacerations.

Ophthalmoscopy

The ophthalmoscope is a hand-held device that resembles a flashlight. It has narrowly focused beam of light and a magnifying lens. The ophthalmologist uses it to examine the inner structures of the back of the eye known collectively as the fundus: the retina, optic disk, and macula. The ophthalmologist usually dilates the pupil for OPHTHALMOSCOPY. This test helps detect numerous problems of the eye including RETINAL DETACHMENT, RETINOPATHY, OPTIC NERVE ATROPHY, and PAPILLITIS. Conditions such as glaucoma cause characteristic changes to the fundus.

Tonometry

The tonometer is a device that measures INTRAOCULAR PRESSURE (the pressure within the eye). The most simple variation involves measuring the force it takes for a puff of air to indent the cornea, a noncontact test. For more accurate results the ophthalmologist numbs the eye with anesthetic drops and touches a TONOMETRY probe against the surface of the eye to measure the pressure. Tonometry is a basic screening test for glaucoma, for which increased intraocular pressure is a key symptom.

See also AMSLER GRID; REFRACTION TEST; SCOTOMA; VISION HEALTH.

ophthalmoscopy Examination of the EYE using an ophthalmoscope, a hand-held, lighted magnifying lens. The ophthalmoscope projects a narrowly

focused beam of light that illuminates the structures of the eye. Ophthalmoscopy is the essential introductory examination of the eye and can determine what, if any, further diagnostic procedures are necessary. Ophthalmoscopy allows the doctor to examine the inner surfaces of the eyelids, general surface of the eye (sclera and CORNEA), pupil response, and iris. It also allows the doctor to visualize the inner structures at the back of the eye, notably the RETINA, optic disk, and macula.

See also OPHTHALMIC EXAMINATION; OTOSCOPY; SLIT LAMP EXAMINATION; TONOMETRY.

optical coherence tomography (OCT) An imaging procedure that noninvasively and painlessly permits the ophthalmologist to visualize the layers of the RETINA. OCT can provide a "virtual biopsy" of retinal tissue, helping diagnose or monitor AGE-RELATED MACULAR DEGENERATION (ARMD), macular holes, retinal tears, and OPTIC NERVE inflammation or damage such as can result from GLAUCOMA. The ophthalmologist can perform OCT in the office; no preparation or recovery is necessary.

See also ELECTRORETINOGRAPHY.

optic nerve The second cranial NERVE, which conveys nerve impulses from the EYE to the BRAIN. There are two optic nerves, one from each eye. The fibers that become the optic nerve originate in the occipital lobes of the cerebrum, in an area called the visual cortex. Each extends along structures called the optic tracts that pass through the temporal lobes and the center of the brain, converging in the optic chiasm. At this point the optic tracts cross, such that the one originating in the left visual cortex goes to the right eye and the one originating in the right visual cortex goes to the left eye. Each optic nerve enters the back of the eye, terminating in the RETINA.

The ophthalmologist can see through the ophthalmoscope the end of the optic nerve, called the optic disk. It appears as a pale circle, about the size of a pencil eraser, against the dark background of the retina. The retina's network of nerves extends from the optic nerve, gathering nerve impulses from the rods, cones, and other nerve cells in the retina.

CONDITIONS THAT CAN AFFECT THE OPTIC NERVE

aging	GLAUCOMA
ISCHEMIC OPTIC NEUROPATHY	TOXIC OPTIC NEUROPATHY
PAPILLEDEMA	PAPILLITIS
RETINAL DETACHMENT	RETINITIS PIGMENTOSA
RETROBULBAR OPTIC NEURITIS	RETINOPATHY

For further discussion of the optic nerve within the context of ophthalmologic structure and function please see the overview section "The Eyes."

See also AGING, VISION AND EYE CHANGES THAT OCCUR WITH; CRANIAL NERVES; ENUCLEATION; OPHTHALMOSCOPY.

optic nerve atrophy Death of NERVE cells within the OPTIC NERVE, affecting the optic nerve's ability to convey nerve signals from the EYE to the BRAIN. Optic nerve atrophy can be partial or complete; when complete there is total loss of vision. Conditions of the eye or systemic neurologic disorders can cause optic nerve atrophy. Symptoms include diminished VISUAL ACUITY and VISUAL FIELD.

CAUSES OF OPTIC NERVE ATROPHY

Eye Conditions	Neurologic or Systemic Conditions
congenital OPTIC NERVE HYPOPLASIA	MULTIPLE SCLEROSIS
ISCHEMIC OPTIC NEUROPATHY	TRAUMATIC BRAIN INJURY (TBI)
congenital CATARACT	STROKE
RETINITIS PIGMENTOSA	methanol poisoning
GLAUCOMA	untreated SYPHILIS

The diagnostic path begins with OPHTHALMOSCOPY, which allows the ophthalmologist to see the visual changes in the optic disk (end point of the optic nerve where it joins the RETINA) that denote its atrophy. Further assessment to determine the cause may include diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) and a comprehensive NEUROLOGIC EXAMINATION. Treatment targets the underlying cause, though it cannot recover vision already lost. Treatment that can halt the causative condition can prevent further loss of vision, though when the cause is a degenerative disorder such as MULTIPLE SCLEROSIS vision loss is likely to continue.

People who smoke cigarettes or consume high quantities of ALCOHOL, particularly in combination, have a higher risk for developing idiopathic optic nerve atrophy (in which the cause remains undetermined. NUTRITIONAL SUPPLEMENTS containing vitamin A and the antioxidants LUTEIN and ZEAXANTHIN may improve visual acuity.

See also OPTIC NERVE HYPOPLASIA; RETROBULBAR OPTIC NEURITIS; TOXIC OPTIC NEUROPATHY.

optic nerve hypoplasia A congenital condition in which the OPTIC NERVE fails to develop completely in the unborn child. Optic NERVE hypoplasia is the third leading cause of congenital vision loss in the United States. The defect is random and may affect one EYE or, more commonly, both eyes. Children who have optic nerve hypoplasia may have barely noticeable to complete VISION IMPAIRMENT depending on the extent to which the optic nerve develops. Diminished peripheral vision and depth perception are common. Typically the pediatrician detects an abnormality of the optic nerve shortly after birth, though mild optic nerve hypoplasia may escape notice until the child begins having vision difficulties. Optic nerve hypoplasia does not progress, so VISUAL ACUITY typically remains stable. CORRECTIVE LENSES may accommodate for vision impairments. Other treatment focuses on teaching the child adaptive methods. There are no known preventive measures.

See also AMBLYOPIA; OPTIC NERVE ATROPHY.

optic neuritis See PAPILLITIS.

orbital cellulitis INFLAMMATION and swelling of the tissues surrounding the EYE, including the eyelids.

Orbital cellulitis requires emergency medical attention. Delayed treatment can result in permanent vision loss.

The most common causes are infections that affect the eyelids such as HORDEOLUM and BLEPHARITIS, DACRYOCYSTITIS (infected tear duct), and infections of adjacent structures such as SINUSITIS (sinus infection), PHARYNGITIS (throat infection), tooth ABSCESS, and occasionally OTITIS media (middle ear infection). Insect bites that become infected also can cause orbital cellulitis. Orbital cellulitis may affect one eye or both eyes, depending on the underlying cause. The eyelids typically swell closed and may appear bruised, with considerable PAIN as well as inability to see. Often there is a moderate FEVER (above 102°F) and EXOPHTHALMOS (bulging of the eye).

The diagnostic path includes assessment of VISUAL ACUITY and VISUAL FIELD, to the extent possible, as well as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to visualize the extent of the infection and determine its site of origin. Treatment is immediate intravenous ANTIBIOTIC MEDICATIONS with hospitalization until fever and swelling subside. Prompt and appropriate treatment improves the likelihood for full recovery and restored vision. Complications can include increased INTRAOCULAR PRESSURE, which is damaging to the RETINA and OPTIC NERVE. Because the optic NERVE presents a direct channel to the BRAIN, INFECTION also may spread to cause MENINGITIS or ENCEPHALITIS.

See also CONJUNCTIVITIS; TRAUMA TO THE EYE.

P

papilledema Swelling of the optic disk, the point at which the OPTIC NERVE enters the RETINA, that results from increased pressure within the skull. Papilledema typically signals serious neurologic damage such as STROKE or TRAUMATIC BRAIN INJURY (TBI) that causes bleeding (HEMORRHAGE), brain tumor, extreme HYPERTENSION, or inflammatory INFECTION such as ENCEPHALITIS and MENINGITIS. Though papilledema is not a disorder of the EYE, untreated it will result in complete loss of vision because the swelling interrupts the flow of blood to the optic NERVE.

Doctors check for any signs of papilledema during a routine OPHTHALMIC EXAMINATION, as often papilledema is an early sign of a neurologic problem. The need for intervention to relieve the intracranial pressure is urgent, not only to preserve vision but also often as a lifesaving measure. The nature of the intervention depends on the underlying cause. Extremely elevated blood pressure points to hypertension as the cause; other causes require NEUROLOGIC EXAMINATION for further evaluation and diagnosis. With prompt treatment to reduce the intracranial pressure, papilledema typically resolves in about six to eight weeks and vision, if affected, returns to its previous level.

Swelling around the optic disk may occur for various reasons that are not the result of increased intracranial pressure. These are usually ophthalmologic in nature, such as GLAUCOMA and ISCHEMIC OPTIC NEUROPATHY. The conditions threaten vision, but they are not life-threatening.

See also OPTIC NERVE ATROPHY; RETROBULBAR OPTIC NEURITIS; TOXIC OPTIC NEUROPATHY.

papillitis INFLAMMATION of the optic disk, the portion of the OPTIC NERVE that enters the RETINA (also called the "blind spot"). Papillitis typically results from, and may be an early diagnostic indicator of, systemic inflammatory conditions such as MULTIPLE SCLEROSIS and temporal arteritis. The inflammation also may follow viral or bacterial INFECTION such as SINUSITIS, especially in children, and occurs rarely as a complication following stings from wasps and bees. Papillitis often affects only one EYE though can involve both eyes. Within hours of its onset the inflammation can cause complete loss of vision in the affected eye. Rapid treatment to reduce the inflammation, or to treat the underlying condition causing the inflammation, can salvage vision. However, loss of vision is often the reason people seek medical attention, by which time there may already be permanent damage to the optic disk. Occasionally the inflammation develops over the course of several weeks, producing progressive loss of vision as well as loss of color perception.

See also BACTERIA; PAPILLEDEMA; RETROBULBAR OPTIC NEURITIS; TOXIC OPTIC NEUROPATHY; VIRUS.

photophobia Heightened sensitivity to bright light, usually the result of INFLAMMATION or irritation to structures of the EYE or with MYDRIASIS (extended dilation of the pupil). Photophobia causes discomfort in the eye ranging from a burning sensation to outright PAIN. Often there is excessive tearing and the eye becomes reddened in response to the irritation. In severe photophobia it may be impossible to keep the eye open. Photophobia is common in the HEALING period following CATARACT EXTRACTION AND LENS REPLACEMENT and CORNEAL TRANSPLANTATION. Photophobia may be a symptom of numerous conditions affecting the eye, including

- CORNEAL INJURY, such as ABRASIONS and burns

- INFECTION, such as BLEPHARITIS, CONJUNCTIVITIS, IRITIS, HORDEOLUM, KERATITIS, UVEITIS
- CHALAZION
- ENTROPION
- Dirty contact lenses or contact lenses worn too long

Photophobia that occurs with FEVER may indicate MENINGITIS and requires emergency medical attention.

The diagnostic path typically includes SLIT LAMP EXAMINATION with FLUORESCEIN STAINING to determine whether there is corneal injury and OPHTHALMOSCOPY to evaluate the structures of the inner eye. These examinations often require anesthetizing drops in the eye to numb the discomfort the lighted instruments cause. Treatment targets the underlying cause, which, when resolved, generally ends the photophobia. ANTIBIOTIC MEDICATIONS, usually ophthalmic solutions or ointment placed in the affected eye, are necessary to treat bacterial infections. Wearing sunglasses to restrict the amount of light that can enter the eye helps reduce the sensitivity response. Some people are naturally photophobic without underlying eye conditions and should wear sunglasses for improved comfort in bright-light settings.

See also BACTERIA; TRAUMA TO THE EYE.

phototherapeutic keratectomy (PTK) Treatment with an excimer (cool) laser to smooth irregularities and dissipate cloudiness in the CORNEA. PTK is an AMBULATORY SURGERY procedure, with local anesthetic to numb the surface of the EYE and a mild sedative for comfort. The procedure takes 20 to 45 minutes, depending on the extent of corneal sculpting needed. The ophthalmologist may prescribe ophthalmic ANTIBIOTIC MEDICATIONS and anti-inflammatory medications after the procedure. Changes in VISUAL ACUITY are generally complete in one to two months.

CONDITIONS PTK CAN TREAT

ASTIGMATISM	corneal clouding
corneal degeneration	corneal dystrophy
corneal scarring	recurrent corneal erosion
recurrent KERATITIS	REFRACTIVE ERRORS

The risks and potential complications of PTK include

- INFECTION
- worsened visual acuity
- RECURRENCE of the original problem

Most people experience improved visual acuity or relief from corneal PAIN following PTK.

See also CORNEAL TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

pinguecula A thickened area of the conjunctival tissue on the EYE, usually forming on the inner (NOSE) side of the eye. A pinguecula may be clear, yellow, or gray in color, and develops slowly. It presents no threat to vision or the eye, and is more common in people over age 50. Many people do not notice that they have pingueculae or consider them normal features of their eyes, though some people experience irritation and a sensation of grittiness in the affected eye. People who spend a lot of time in the sun or have other long-term ultraviolet light exposure are more likely to develop a pinguecula. Ophthalmologists recommend wearing sunglasses or protective eyewear that filters ultraviolet light. There is no reason to treat a pinguecula unless it puts pressure on the CORNEA or otherwise interferes with vision.

See also CONJUNCTIVITIS; PTERYGIUM; SCLERITIS.

presbyopia A progressive change in the eyes that occurs with aging, in which it becomes increasingly difficult to focus on near objects. Presbyopia occurs because the LENS loses FLEXIBILITY, limiting its ability to adjust between near and far focus. The lens becomes unable to contract to thicken in the center as near focus requires, resulting in the inability to see objects that are close, such as when reading. Most people begin to notice presbyopia when they reach their mid-40s in age. People who have MYOPIA (nearsightedness) may also find that their distant vision improves as presbyopia advances. The EYE changes responsible for presbyopia reach their end point by about the mid-50s, after which the stiffening of the lens stabilizes. Eyeglasses, contact lenses, and surgery offer options for correcting presbyopia.

Eyeglasses

The conventional treatment for presbyopia is reading glasses, which are magnifying lenses that enlarge near objects to allow the eyes to focus on them. Many retail and optical stores sell standard reading glasses that come in common magnifications typically ranging from +1.00 to +3.00 in gradations of 0.25 power. This is often the least expensive and most convenient option. An optometrist also can prescribe custom-strength lenses.

People whose eyes otherwise do not require refractive correction wear reading glasses as needed for close vision. People who have other REFRACTIVE ERRORS, such as myopia or ASTIGMATISM, and wear eyeglasses require bifocal or trifocal CORRECTIVE LENSES that provide multiple levels of correction to accommodate both the refractive correction and the magnification for close vision. Eyeglass lenses may be progressive, in which there are no discernible lines on the lens to mark the transition from one level to another. People who wear contact lenses to correct refractive errors often choose to wear reading glasses as needed with the contacts for close vision, or may choose to switch to eyeglasses.

Contact Lenses

Contact lenses may also have multiple levels of refractive correction (multifocal contact lenses). Another approach using contact lenses is monovision, in which one eye, typically the dominant eye, wears a lens that fully corrects for refractive error and the other eye wears a lens that undercorrects. The BRAIN learns to distinguish which eye to use for close and for distant focusing, automatically shifting as necessary. It may take a week or two for the brain to make the adjustment and for monovision to feel comfortable. However, some people do not adjust to monovision at all. Monovision results in some loss of depth perception, which some people find barely noticeable and other people find intolerable.

Surgery

In the United States, the two most commonly used surgical methods to correct presbyopia are conductive keratoplasty and LASIK (an acronym for laser-assisted in situ keratomileusis), both done as ambulatory procedures that require no overnight hospital stay. In conductive keratoplasty, the ophthalmologist uses radiofrequency energy applied in a concentric pattern around the base of the CORNEA to shrink corneal collagen. This constricts the cornea's base, causing the center of the cornea to thicken and rise, which improves close focus. It may take several weeks to experience the full effect. In LASIK, the ophthalmologist uses an excimer laser to reshape the cornea. There is little recovery time with LASIK, and effects are apparent almost immediately.

Each surgical method establishes a permanent degree of monovision. Depending on the age of the person and the anticipated progression of the presbyopia, the ophthalmologist may leave a margin of correction to allow for future changes. Many ophthalmologists recommend a trial of monovision with contact lenses before surgery to determine whether the approach produces acceptable results. The risks of surgical correction for presbyopia include INFECTION, vision that still requires corrective lenses even after surgery, and, rarely, worsened vision. Some people may have other eye conditions, vision problems, or general health conditions that exclude them from surgery as an option to correct presbyopia.

See also HYPEROPIA; REFRACTIVE SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

prosthetic eye A cosmetic replacement, also called an ocular prosthesis or artificial EYE, for a surgically removed (enucleated) eye. A specialist called an ocularist designs the prosthetic eye to be as close a match in appearance as possible for the remaining natural eye.

The most common type of prosthetic eye attaches to a spherical implant the same size and shape of the eye that the surgeon places in the orbit (eye socket) after removing the eye. As the HEALING process takes place, other tissues and blood vessels grow into and around the implant, anchoring it firmly within the orbit. Once healing is complete, the surgeon drills into the front of the implant to attach a small post. The post then holds the prosthetic eye, a "facing" that fits over the front of the implant. The muscles of the orbit move the implant in coordination with the movements of the healthy eye, providing a natural appearance to the prosthetic eye.

Another type of ocular prosthesis is a scleral shell, which covers a dysfunctional and disfigured eye that remains in place. The scleral shell is somewhat like an oversize contact lens, fitted to rest on the eye as does a contact lens. The ocularist designs the front of the shell to match the appearance of the other eye. Because the scleral shell rests on the surface of the eye, it moves in synchronization with the other eye for a natural appearance.

Over time the orbital structures change and the materials of the prosthetic eye experience some natural deterioration. Most people need to replace the prosthetic eye every two years, though the implant is permanent. Children may need more frequent replacements to keep pace with their growth. The prosthesis requires regular care and cleaning.

See also ENUCLEATION.

pterygium A growth arising from the conjunctival tissue around the perimeter of the EYE, usually on the side near the NOSE. A pterygium characteristically grows in a triangular shape, and has its own BLOOD supply to support its growth. Growth generally is slow. Often a pterygium remains innocuous, though some people experience irritation and a sensation of grittiness in the affected eye. Occasionally the growth encroaches on the CORNEA, applying pressure or growing into the corneal region. When this occurs, surgery to remove the pterygium is necessary to preserve vision. Pterygia tend to recur following surgery, though it may take a number of years to reach a size that interferes with vision.

See also CONJUNCTIVITIS; PINGUECULA; SCLERITIS.

ptosis Drooping of the upper eyelid. Ptosis often is a consequence of MUSCLE weakness or neurologic damage, and is sometimes a symptom of a neurologic condition such as MYASTHENIA GRAVIS or MUSCULAR DYSTROPHY. Ptosis may be congenital (present at birth), the result of underdevelopment or absence of the levator muscle that raises the eyelid. Ptosis also may develop with advanced age, reflecting weakening of the muscles that control the eyelid.

When the drooping obscures vision, surgery to raise the eyelid is necessary to prevent AMBLYOPIA. Surgery may result in a slight asymmetry in the movements of the upper eyelids, particularly in congenital ptosis, when the levator muscle is missing and the surgeon must configure eyelid movement to make use of other muscles. Generally no treatment is necessary when the ptosis does not interfere with vision, except as desired for cosmetic purposes.

See also BLEPHARITIS; BLEPHAROPLASTY; ECTROPION.

R

refraction test A diagnostic procedure to measure REFRACTIVE ERRORS of the EYE, such as MYOPIA, HYPEROPIA, and ASTIGMATISM. An optometrist or ophthalmologist conducts the test using a device called a refractor. The refractor fits against the face somewhat like a flattened pair of binoculars, with a chin rest and forehead pad to support the head in proper position. After covering one eye, the eye professional applies combinations of lenses to the eye piece. The person looks through the eye piece and lens at a rendition of the SNELLEN CHART. The eye professional examines first one eye with the other eye covered, switches eyes, and finally examines both eyes together to confirm the appropriate refractive correction.

See also CORRECTIVE LENSES; OPHTHALMIC EXAMINATION.

refractive errors Vision disorders in which a defect of the EYE does not allow proper refraction of light. When the eye is longer than normal from front to rear, the lightwaves entering the eye focus short of the RETINA, resulting in MYOPIA (nearsightedness). When the eye is shorter, the lightwaves that enter the eye focus behind the retina, resulting in HYPEROPIA (farsightedness). An irregular surface or shape to the cornea may produce distortions of refraction, resulting in ASTIGMATISM. The optometrist or ophthalmologist measures refractive errors using a refraction test. Treatment is CORRECTIVE LENSES (eyeglasses or contact lenses) or REFRACTIVE SURGERY. Refractive errors may change frequently during childhood, though usually stabilize by early adulthood. Severe refractive errors may be uncorrectable, notably myopia, resulting in functional or legal blindness.

See also PRESBYOPIA; VISION IMPAIRMENT.

refractive surgery Operations to correct REFRACTIVE ERRORS of vision such as MYOPIA (nearsightedness), HYPEROPIA (farsightedness), and ASTIGMATISM (irregularity of the CORNEA). Refractive surgery became an option for permanent refractive correction in the United States in the 1980s, following its introduction and rapid growth in popularity in Europe. Now, about 1.5 million Americans undergo refractive surgery operations each year.

Surgical Procedure

There are numerous refractive surgery techniques in use today. They fall into the general categories of those that use lasers, those that use microkeratomes (specialized blades), and those that use implants to alter the eye's natural structure. There are five commonly performed refractive correction operations:

- LASIK (laser-assisted in situ keratomileusis) has become the standard procedure for most refractive corrections. The EYE surgeon makes a small flap to expose the inner portion of the cornea, uses an excimer (cool) laser to remove microscopically thin layers of corneal tissue, and replaces the corneal flap. Because the surface of the cornea, which contains NERVE endings, remains intact, there is almost no postoperative discomfort and results are immediately apparent. LASIK is most effective for hyperopia, astigmatism, and moderate myopia.
- Photorefractive keratectomy (PRK) was the original refractive LASER SURGERY. The eye surgeon uses an excimer laser to reshape the surface of the cornea. Results are not apparent until the cornea heals, which takes several weeks. There is some discomfort during the

HEALING phase. PRK is particularly effective for people who have large pupils or thin corneas, because it does not create a corneal flap, which reduces the likelihood of postoperative glare and halos at night.

- Automated lamellar keratoplasty (ALK) is similar in concept to LASIK, though the surgeon uses a microkeratome, a specialized surgical blade. The eye surgeon makes a flap in the cornea and removes minute segments of corneal tissue, then replaces the flap. As with LASIK, there is little discomfort during healing and results are apparent immediately. ALK is particularly successful for severe myopia.
- LENS replacement uses techniques perfected through 60 years of CATARACT EXTRACTION AND LENS REPLACEMENT surgery. The eye surgeon removes the natural lens and replaces it with one curved to accommodate for severe hyperopia or myopia. Multifocal lens implants allow the eye to adjust between close and distant vision.
- Phakic intraocular contact lens implantation places a permanent contact lens in front of or behind the natural lens to supplement its focusing ability. This approach preserves the focusing ability of the natural lens.

The eye surgeon may choose other methods, depending on an individual's refractive situation, age, and general health status. Not everyone with refractive errors is a good candidate for refractive surgery. It is important to consult with a qualified and experienced eye surgeon and to understand the potential risks and benefits of the different operations. Refractive surgery permanently alters the eye's structure, although subsequent operations can often refine the effects when they are not as expected. Severe refractive errors may require multiple procedures.

Risks and Complications

As with any surgery, a potential complication of refractive surgery is postoperative INFECTION that can range from mild discomfort to significant damage to the eye with resulting VISION IMPAIRMENT. Prompt treatment prevents further complications. Most eye surgeons have stringent follow-up procedures intended to detect operative complications before they cause eye problems; it is important to maintain the recommended follow-up procedures. Other common complications include dry eyes and seeing halos around lights at night. Procedures involving lens replacement carry the additional risks of excessive bleeding and RETINAL DETACHMENT, which can compromise vision. Complications particular to LASIK include irregularity in the corneal surface after the corneal flap heals and overgrowth of corneal tissue that requires subsequent surgery to remove.

Occasionally the outcome is not as desired or expected, perhaps as a consequence of complications during the operation or during the healing process. It is important for the eye surgeon to appropriately match the person with the procedure, which takes into consideration the nature and severity of the refractive error, the person's age and general health status, and the person's expectations. Despite the precision of computer-guided procedures, there remains an element of unpredictability that influences outcome. Some people may find their vision undercorrected and others overcorrected as a consequence of individual variation in eye structure, refractive error, and healing process.

Though the changes of refractive surgery are permanent, the effects on vision are not. Everyone eventually acquires PRESBYOPIA, a decrease in the ability to focus on near objects that is a function of change that occurs with aging. People who have had refractive surgery to correct astigmatism, hyperopia, or myopia will still need corrective measures for close vision as presbyopia develops. Nonsurgical solutions for presbyopia include contact lenses or reading glasses. Surgical solutions for presbyopia currently employ an approach called monovision, in which the eye surgeon undercorrects the vision in one eye for near focus. The refractive correction for the other eye is full, allowing for distant focus. The BRAIN does the work of switching between the eyes according to the vision needs.

Outlook and Lifestyle Modifications

Refractive surgery dramatically improves visual acuity for nearly everyone who has a successful surgical experience—that is, was properly

matched to the correct procedure, had the operation performed by a competent and experienced eye surgeon, and had an uncomplicated course of recovery. Some people are able to completely eliminate the need for corrective lenses. Many people do still require corrective lenses, though at much improved refractive correction and perhaps only for specific applications such as near or midrange vision.

Doctors do not know what, if any, long-term consequences may result from refractive surgery, as most of the laser techniques predominantly in use today have been available only since the 1990s. Routine eye care and ophthalmic examinations are especially important for people who have had surgery on their eyes, to detect complications from the surgery as well as eye conditions such as GLAUCOMA, AGE-RELATED MACULAR DEGENERATION (ARMD), and CATARACT.

See also AMBULATORY SURGERY; CORNEAL TRANSPLANTATION; OPERATION; PHOTOTHERAPEUTIC KERATECTOMY (PTK); SURGERY BENEFIT AND RISK ASSESSMENT.

retina The innermost layer of the EYE. The retina receives light images and converts them to NERVE impulses the OPTIC NERVE conveys to the BRAIN. The retina is two tissue-thin layers that together are less than ½ millimeter in thickness. The outer pigment layer provides a completely light-absorbing, nonreflective lining. The inner sensory layer contains the photoreceptors (rods and cones) responsible for vision. Rods detect only shades of gray though can register images of very low intensity. Cones detect color and detail.

Laid out flat, like a disk, the retina measures just under 2 inches in diameter. The primary work of vision takes place in an area about the size of a postage stamp called the macula. Most of the retina's 120 million rods and 6 million cones reside in the macula. A section of the central retina no larger than a pencil eraser, the macula, contains almost no rods and an abundance of cones and handles detail vision. A pencil-point depression within the macula, the fovea, has the highest concentration of cones.

The optic nerve enters the retina somewhat to the NOSE-side at the back of the eye, along with the ARTERY and VEIN that manage the retina's BLOOD supply. Vitreous humor, a gelatinous substance, fills the inner eye and holds pressure against the retina, keeping it smoothly and tightly adhered to the choroid.

The ophthalmologist can examine the surface of the retina using OPHTHALMOSCOPY. Under illumination the retina appears reddish orange. The optic nerve disk appears as a pale, pinkish circle. The macula, of similar size, appears as a darker and less distinct circular area with a depression, the fovea, in its center.

CONDITIONS THAT CAN AFFECT THE RETINA

AGE-RELATED MACULAR DEGENERATION (ARMD)	COLOR DEFICIENCY
NIGHT BLINDNESS	COLOR DEFICIENCY
RETINITIS PIGMENTOSA	RETINAL DETACHMENT
RETINOPATHY	RETINOBLASTOMA
	traumatic injury

For further discussion of the retina within the context of eye structure and function please see the overview section "The Eyes."

See also ELECTRORETINOGRAPHY; FLASHES; LENS; VISION IMPAIRMENT; VITREOUS DETACHMENT.

retinal detachment A separation of the RETINA from the choroid, the layer of the EYE's structure that nourishes and attaches the retina. Retinal detachment may occur as a result of TRAUMA TO THE EYE, AGE-RELATED MACULAR DEGENERATION (ARMD), VITREOUS DETACHMENT, RETINOPATHY of DIABETES, or surgery on the eye. Retinal detachment may also occur spontaneously, a circumstance more common in people with moderate to severe MYOPIA (nearsightedness).

Prompt treatment to reattach the retina is necessary to save vision.

Symptoms and Diagnostic Path

Retinal detachment does not cause PAIN or discomfort. Detachment may be gradual, in which case symptoms are progressive, or sudden, in which case loss of vision may be the only symptom. Symptoms of retinal detachment include

- seeing flashing lights or multiple FLOATERS
- the perception of a curtain or shadow dropping across the VISUAL FIELD, often from top to bottom though sometimes from the side

- blurred vision
- loss of VISUAL ACUITY

OPHTHALMOSCOPY to examine the interior of the eye provides the diagnosis.

Treatment Options and Outlook

Most often, the preferred treatment for reattaching the retina is surgery. The surgeon may use laser, photocoagulation (heat), or cryotherapy (freezing) techniques. Other approaches include injecting sterile silicone oil into the inner eye or injecting a sterile gas bubble (pneumotherapy) into the vitreous humor to hold the retina in place with pressure. A rapidly reattached retina often fully recovers without measurable loss of vision. Delay in reattaching the retina, or when the retina suddenly and completely detaches, often results in less successful vision preservation. An untreated retinal detachment results in permanent, complete loss of vision in the eye.

Risk Factors and Preventive Measures

People who have moderate to severe myopia (greater than – 8 diopters) are at increased risk for retinal detachment because of the eye's shortened length. Retinal detachment is also a complication of LASIK surgery, CATARACT EXTRACTION AND LENS REPLACEMENT surgery, and serious inflammatory conditions of the eye such as SCLERITIS. Retinopathy, in which extra blood vessels grow into the retina, also increases the risk for retinal detachment. Protective eyewear to reduce the risk of trauma to the eye can prevent trauma-related retinal detachment. In other circumstances, early detection and reattachment are the most effective measures to preserve vision.

See also LASER SURGERY; OPERATION; REFRACTIVE SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

retinitis pigmentosa The collective term for a group of hereditary disorders that result in progressive loss of vision. Retinitis pigmentosa generally begins with diminished night vision, as the degeneration affects primarily the rods (photoreceptors responsible for vision in dim light and for peripheral vision). Eventually the condition progresses to rods, and then cones, throughout the RETINA. In most people symptoms begin between the ages of 10 and 30, with complete loss of vision by around age 40.

When viewed through the ophthalmoscope, the areas of degeneration appear darker than the surrounding areas of retina. The diagnostic path may also include a DARK ADAPTATION TEST and ELECTRORETINOGRAPHY. There is no known treatment for retinitis pigmentosa. Several INHERITANCE PATTERNS are responsible for retinitis pigmentosa; doctors recommend GENETIC TESTING and GENETIC COUNSELING for family members when there is a diagnosis of this condition. Retinitis pigmentosa also may accompany a number of other hereditary syndromes.

See also COLOR DEFICIENCY; NIGHT BLINDNESS; OPHTHALMOSCOPY; RETINOPATHY; VISION IMPAIRMENT.

retinoblastoma A cancerous tumor of the RETINA that most often occurs in children. Most retinoblastomas are hereditary and develop in early childhood, usually by age four. Some retinoblastomas are the result of new germline mutations though are not hereditary. About 70 percent of retinoblastomas involve only one EYE. Treatment in such cases is surgery to remove the EYE (ENUCLEATION), with placement of a PROSTHETIC EYE for cosmetic reasons. When retinoblastoma is bilateral (involves both eyes), treatment attempts to save vision while eradicating the CANCER. Treatment for bilateral retinoblastoma may include enucleation of one eye and cryotherapy or photocoagulation to reduce as much as possible the tumor in the other eye, with follow-up CHEMOTHERAPY or RADIATION THERAPY. Treatment is successful in about 90 percent of children when doctors detect the tumor before it metastasized beyond the eye. However, about 70 percent will experience second retinoblastomas by adulthood.

See also ADULT SURVIVORS OF CHILDHOOD CANCER; CANCER TREATMENT OPTIONS AND DECISIONS; GENE TESTING; GENETIC COUNSELING.

retinopathy A dysfunction of the RETINA in which new BLOOD vessels grow across the retina's surface. This growth causes the death of photoreceptors, the specialized cells (rods and cones) in the retina that receive lightwaves and convert them to NERVE impulses for transmission to the BRAIN. The blood vessels are also delicate and

prone to bleeding, which further damages the surface of the retina. The most common forms of retinopathy are the following:

- Retinopathy of DIABETES results from chronically elevated blood GLUCOSE levels. Retinopathy of diabetes takes one of two forms: proliferative, in which the new blood vessels that grow across the retina are unstable and bleed, or nonproliferative, in which existing blood vessels deteriorate and form aneurysms that rupture and bleed. Retinopathy of diabetes typically develops over decades, is more common in people who require INSULIN THERAPY, and is the most common cause of blindness in people under age 60.
- Retinopathy of prematurity occurs in some infants born earlier than 32 weeks of gestational age in whom the retinal blood vessels, which develop late in gestation, have not yet formed. In most infants, the blood vessels resume growth and establish normal retinal vasculature with no damage to vision. In some premature infants who have retinopathy, inadequate blood supply to the retina or abnormal vessel development can cause RETINAL DETACHMENT with resulting VISION IMPAIRMENT.
- Hypertensive retinopathy develops as a consequence of untreated or poorly managed HYPERTENSION (high BLOOD PRESSURE). Blood vessels in the retina, like blood vessels throughout the body, become stiff and inflexible as a result of the continuous pressure. This brittleness makes them susceptible to rupture, which floods the retina with blood.
- Central serous retinopathy, in which fluid accumulates between the retina and the choroid, causes the retina to swell and lift up from the choroid.

Symptoms and Diagnostic Path

Most often, retinopathy does not cause symptoms until eye damage becomes significant. When symptoms are present, they may include

- blurred or distorted vision
- diminished near vision for reading and other close focus
- FLASHES and FLOATERS
- sudden loss of vision

OPHTHALMOSCOPY typically reveals discolored areas of the retina that indicate diminished blood supply (pale) or bleeding (dark). The ophthalmologist may also be able to see frank bleeding or irregularities in the surface of the retina that indicate accumulated fluid. When the cause of the retinopathy is hypertension, there may also be PAPILLEDEMA (swelling of the OPTIC NERVE). Ophthalmoscopy in combination with health history generally provides the information the ophthalmologist needs to make the diagnosis.

Treatment Options and Outlook

Often retinopathy improves on its own, especially retinopathy of prematurity and central serous retinopathy. Retinopathy of diabetes or hypertension typically improves with tighter control of the underlying condition. When retinopathy improves, vision may return to its previous state or damage to vision may be minimal. Retinopathy that progresses leads to vision impairment, including total loss of vision. Central serous retinopathy tends to recur. Proliferative and nonproliferative retinopathy often require laser treatment.

Risk Factors and Preventive Measures

The key risk factors for most retinopathy are the underlying health conditions associated with the retinopathy. Preventive measures emphasize control of the underlying condition—maintaining stable blood glucose levels in retinopathy of diabetes, and healthy blood pressure in retinopathy of hypertension. Consistent PRENATAL CARE and attention to maternal health (notably SMOKING CESSATION) help reduce the risk for PREMATURE BIRTH. Regular ophthalmic examinations can detect retinopathy in its early stages, allowing therapeutic interventions to minimize damage to the eye.

See also ISCHEMIC OPTIC NEUROPATHY; RETINITIS PIGMENTOSA; TOXIC OPTIC NEUROPATHY.

retrobulbar optic neuritis INFLAMMATION of the OPTIC NERVE outside the globe of the EYE, between the eye and the BRAIN. Retrobulbar optic neuritis can result from INFECTION such as MENINGITIS or ENCEPHALITIS, as a consequence of toxic exposure,

and as a manifestation of MULTIPLE SCLEROSIS. Symptoms may include

- PAIN with eye movement
- diminished VISUAL ACUITY (blurred or dim vision)
- eye is tender to touch or pressure
- blind spots (scotomas)
- dulled colors

The diagnostic path includes visual acuity and VISUAL FIELD testing, OPHTHALMOSCOPY to examine the optic NERVE disk (which often becomes more pale), and MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN of the brain when the doctor suspects multiple sclerosis or another neurologic cause. Most retrobulbar optic neuritis eventually goes away without treatment. The doctor may prescribe CORTICOSTEROID MEDICATIONS when the inflammation persists. Because retrobulbar optic neuritis is so often associated with multiple sclerosis, the doctor may recommend more extensive NEUROLOGIC EXAMINATION to determine whether this condition is the underlying cause. Recurrent or severe retrobulbar optic neuritis may result in permanent VISION IMPAIRMENT.

See also OPTIC NERVE ATROPHY; OPTIC NERVE HYPOPLASIA; PAPILLITIS; SCOTOMA; TOXIC OPTIC NEUROPATHY.

S

scleritis An INFLAMMATION of the sclera, the white fibrous outer layer of the EYE. The inflammation develops gradually, involving the connective tissue structure of the sclera. The scleritis may involve a small portion of the sclera (sectoral scleritis) or the entire globe of the eye (diffuse scleritis). Some people develop nodules that may become necrotic (cause tissue death). Necrotizing scleritis, with or without nodules, results in severe damage to the eye (including perforation) and often loss of vision. More than half of the people who develop scleritis also have connective tissue disorders, the most common associations being with RHEUMATOID ARTHRITIS and VASCULITIS.

CONDITIONS OFTEN ASSOCIATED WITH SCLERITIS

ANKYLOSING SPONDYLITIS	RHEUMATOID ARTHRITIS
SARCOIDOSIS	SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
VASCULITIS	Wegener's granulomatosis

Deep, aching PAIN characterizes scleritis, often severe enough to disrupt sleep. Referred pain sometimes affects the jaw or cranial bones around the eye. The affected area of the sclera is erythematous ("bloodshot"), and the eye typically tears in response to light (PHOTOPHOBIA). The eye may protrude from the front of the orbit when scleritis involves the back of the eye. The diagnostic path typically includes SLIT LAMP EXAMINATION and OPHTHALMOSCOPY, and possibly ULTRASOUND to determine whether the inflammation involves the back of the eye.

Treatment is topical CORTICOSTEROID MEDICATIONS and oral NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which suppress inflammation as well as relieve pain. Eye drops to constrict the blood vessels in the eye reduce swelling and redness. Diffuse or severe inflammation may require a therapeutic course of systemic corticosteroid medication such as prednisone. Prompt diagnosis and treatment can preserve the eye and vision. However, permanent structural damage to the eye with resulting loss of vision is a significant risk even with treatment. Scleritis may recur when it is a manifestation of an underlying connective tissue or AUTOIMMUNE DISORDER.

See also CONJUNCTIVITIS; EPISCLERITIS; KERATITIS; UVEITIS; VISION IMPAIRMENT.

scotoma An area of the RETINA in which there are few or no cones or rods, the specialized NERVE cells that convert light signals to nerve impulses, creating a blind spot in the VISUAL FIELD. Scotomas may represent healed injuries to the retina such as retinal tears or degeneration of the retina such as may occur with AGE-RELATED MACULAR DEGENERATION (ARMD) or GLAUCOMA. A simple test called the AMSLER GRID, a grid of equally spaced vertical and horizontal lines, detects scotomas.

See also RETINOPATHY.

slit lamp examination The examination of the outer EYE using a bright light focused into an elongated slit in combination with a biomicroscope. The examination takes place in a darkened room, with the person sitting on one side of the slit lamp and the ophthalmologist on the other side. The ophthalmologist moves the light across the surface of the eye to examine the inner eyelids, sclera, CORNEA, iris, and LENS. The ophthalmologist may also put drops in the eyes to dilate the pupils, then use the slit lamp to examine the structures at the back of the eye, such as the RETINA and OPTIC NERVE, as well. The bright light of the slit lamp is sometimes uncomfortable as it passes across the eye, especially with dilated pupils that allow the full

intensity of the light to enter the inner eye. The examination takes only a few minutes.

See also OPHTHALMIC EXAMINATION; OPHTHALMOSCOPY.

Snellen chart The familiar eye chart, featuring lines of letters and numbers that progressively decrease in size, to assess VISUAL ACUITY. Dutch ophthalmologist Herman Snellen (1834–1908) developed the chart in the 1860s. The top letter is typically E. A person with normal vision can read a one-inch letter from 20 feet away, designated as 20/20 vision. Each line on the chart represents a ratio of normal vision. A person who can see at 20 feet what someone who has normal vision could see at 60 feet has 20/60 vision. A REFRACTION TEST then determines the precise correction necessary to bring visual acuity as close to 20/20 as possible. To take a Snellen test, a person reads the smallest line possible with each eye separately (one eye covered) and both eyes together.

See also AMSLER GRID; OPHTHALMIC EXAMINATION; VISION IMPAIRMENT.

strabismus A condition, also called tropia, in which the eyes do not focus simultaneously on the same object. One EYE may turn inward ("cross-eye" or esotropia), or one eye may turn outward ("walleye" or exotropia). Congenital strabismus may occur with RETINOBLASTOMA or RETINOPATHY of prematurity and becomes apparent in the first few months after birth. Most strabismus develops in children between the ages of one and five. About half of the time the cause of strabismus in children is unknown (idiopathic) and not associated with any underlying condition.

In adults, strabismus may develop as a consequence of TRAUMA TO THE EYE, TRAUMATIC BRAIN INJURY (TBI), or STROKE. Adults may experience double vision (DIPLOPIA) or uncoordinated movements of the eyes. Adults also may acquire strabismus as a consequence of vision loss in one eye, which results in lack of visual signals that cue the BRAIN for MUSCLE movements of the eye. Common causes of acquired strabismus in adults include stroke, trauma, GRAVES'S DISEASE, and other surgery.

The diagnostic path includes comprehensive ophthalmic and NEUROLOGIC EXAMINATIONS. Timely treatment in children is essential to prevent AMBLYOPIA, in which the brain learns to perceive images from only one eye. This learning establishes the brain's vision pathways, and if untreated becomes a form of permanent vision loss. Strabismus treatment may include exercises or surgery to strengthen the eye muscles of the weak eye.

See also GRAVES'S OPTHALMOPATHY; OPHTHALMIC EXAMINATION; VISION IMPAIRMENT.

stye See HORDEOLUM.

T

tonometry A test that measures INTRAOCULAR PRESSURE (the pressure within the EYE). The primary reason for tonometry is to screen for GLAUCOMA, a condition for which elevated intraocular pressure is a characteristic symptom. Increased intraocular pressure is also common with ORBITAL CELLULITIS and GRAVES'S OPHTHALMOPATHY. Tonometry is a standard component of the OPHTHALMIC EXAMINATION.

There are several methods of tonometry. The most commonly used are

- applanation, in which the ophthalmologist puts anesthetic drops in the eyes and then touches a device called a tonometer to the surface of the CORNEA to measure how much pressure it takes to depress the cornea
- noncontact, or air puff, in which the person stares at a focused light while a device blows a quick puff of air at the cornea, then measures the change in reflected light from the cornea

Elevated intraocular pressure, or intraocular HYPERTENSION, requires further evaluation to detect and correct the cause. Intraocular pressure that remains elevated damages or destroys the OPTIC NERVE, resulting in total vision loss in the affected eye.

See also OPHTHALMOSCOPY; SLIT LAMP EXAMINATION.

toxic optic neuropathy Damage to the OPTIC NERVE, RETINA, and other structures of the EYE as a SIDE EFFECT of medications or exposure to environmental or systemic toxins. Many substances can harm vision, and any substance that is a neurotoxin (damaging to the NERVOUS SYSTEM) has the potential to damage the optic nerve. Long-term cigarette smoking or ALCOHOL abuse, and especially a combination of these practices, causes various disturbances of vision and ocular function. Severe or chronic MALNUTRITION, notably vitamin B_{12} deficiency, also results in toxic optic neuropathy. As well, numerous medications cause temporary visual disturbances, among them sildenafil (color shifts) and antidepressants (distorted perception and VISUAL ACUITY).

POSSIBLE SOURCES OF TOXIC OPTIC NEUROPATHY

amiodarone	carbon monoxide
chloroquine	digoxin
ethambutol	ethanol (drinking ALCOHOL)
ethylene glycol (antifreeze)	industrial chemicals
isoniazid	lead
mercury	methanol (wood ALCOHOL)
methotrexate	NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)
pyridoxine	quinine
radiation exposure	sulfonamide
tamoxifen	tobacco use
ultraviolet light	

Symptoms and Diagnostic Path

Most often toxic optic neuropathy develops slowly as the consequence of cumulative exposure. Symptoms may include

- dimness and diminished clarity
- altered color perceptions (dyschromatopsia)
- blind spots in the visual field (SCOTOMA)
- PHOTOPHOBIA (extreme sensitivity to light)
- DIPLOPIA (double vision)

Symptoms progressively worsen with continued exposure to the toxic substance. Symptoms may begin in one eye though nearly always

involve both eyes as the effects of the toxic exposure continue to develop.

Treatment Options and Outlook

Treatment is immediate cessation of exposure to the causative agent, though it is unwise and potentially harmful for individuals to stop taking prescribed medications without consulting their physicians. In many circumstances the damage is reversible and normal vision returns after exposure to the toxin ends, though it may take several weeks to several months for the damage to heal.

Risk Factors and Preventive Measures

The primary risk for toxic optic neuropathy is exposure to ocular toxins. Because these are numerous and may be prescription or over-the-counter medications, it is important to know the possible side effects of all medications individually as well as in combination. Avoiding ocular toxins or stopping medications that cause vision disturbances helps prevent permanent damage to the eyes.

See also GRAVES'S OPHTHALMOPATHY; ISCHEMIC OPTIC NEUROPATHY; OTOTOXICITY.

tropia See STRABISMUS.

uveitis INFLAMMATION of the uveal structures of the EYE, which include the iris, ciliary body, and choroid. Uveitis most commonly affects the front of the eye (anterior uveitis) though may involve specific segments of the eye or the uveal tract throughout the eye (diffuse uveitis). Symptoms can vary from mild to severe and may include blurred vision, PHOTOPHOBIA (extreme sensitivity to light), burning sensation, prominent blood vessels ("bloodshot" appearance) radiating from the iris into the sclera, excessive tearing, and PAIN. GLAUCOMA is a serious potential complication of uveitis that can lead to VISION IMPAIRMENT.

The diagnostic path includes SLIT LAMP EXAMINATION and OPHTHALMOSCOPY. Treatment includes cycloplegic drops to immobilize the iris, which helps subdue the inflammation, and corticosteroid drops. Some people need to use corticosteroid drops up to several months. With prompt treatment, most people recover fully and without damage to the eye or to vision. Chronic uveitis may occur with certain AUTOIMMUNE DISORDERS such as INFLAMMATORY BOWEL DISEASE (IBD), RHEUMATOID ARTHRITIS, and REITER'S SYNDROME.

See also CONJUNCTIVITIS; CORTICOSTEROID MEDICATIONS; EPISCLERITIS; PAPILLITIS; SCLERITIS.

V–X

visual acuity The ability to see objects clearly and sharply. Visual acuity assesses central vision and represents the function of the CORNEA, iris (pupil size), LENS, and RETINA. The SNELLEN CHART, which presents lines of letters of diminishing size, is the standard measure of visual acuity. Environmental factors that influence visual acuity include lighting and contrast. The most common disturbances of visual acuity are REFRACTIVE ERRORS such as MYOPIA (nearsightedness), HYPEROPIA (farsightedness), and ASTIGMATISM (blurred vision). PRESBYOPIA, age-related changes in the cornea's FLEXIBILITY, affects near-vision visual acuity.

See also NIGHT BLINDNESS; VISION IMPAIRMENT.

visual field The total area or scope of vision. EYE care specialists map the visual field by measuring the boundaries of peripheral vision in degrees from the point of central vision. A normal field of vision is 135 degrees vertically (60 degrees up and 75 degrees down) and 160 degrees horizontally (100 degrees outward and 60 degrees inward). Everyone has a blind spot of about 10 degrees in the direct center of vision, the point at which the OPTIC NERVE enters the RETINA (the optic disk). The optic disk contains no rods or cones. Binocular vision (the ability to see with both eyes) compensates for each eye's blind spot with overlapping visual fields for each eye. People who have monocular vision (the ability to see only through one eye) learn to accommodate for the blind spot by frequently moving the eye to scan the field of vision.

There are several methods for measuring visual field. The simplest though least precise is for the eye care specialist to sit across from the person and, with the person looking at a fixed point the eye care specialist slowly moves a hand or an object such as a pen. The person tells the point at which he or she can see the object. The eye care specialist may repeat this procedure several times for each eye, measuring peripheral vision from each side, above, and below. Other methods may use computerized flashing lights with the person looking at a fixed point (target) within a contained dome. The person presses a button for each light he or she sees, and the eye care specialist creates a map of each eye's visual field that allows calculation of visual field percentages.

CONDITIONS THAT CAN AFFECT THE VISUAL FIELD

AGE-RELATED MACULAR DEGENERATION (ARMD)	DIABETES
GLAUCOMA	GRAVES'S OPHTHALMOPATHY
HYPERTENSION	MULTIPLE SCLEROSIS
RETINAL DETACHMENT	RETINITIS PIGMENTOSA
RETINOPATHY	SCLERITIS
STROKE	TRAUMA TO THE EYE
	tumors of the eye or BRAIN

See also AMSLER GRID; REFRACTION TEST; SCOTOMA; SNELLEN CHART; VISUAL ACUITY.

vision health Personal care for the eyes to protect the eyes and preserve vision. The two most important elements of vision health are EYE protection and regular ophthalmic examinations.

Protective Eyewear

Most injuries to the eyes are preventable by wearing appropriate protective eyewear, which ranges from sunglasses to protect the eyes from sunburn to specialized eyewear for specific needs. Such needs might include

- ultraviolet exposure (sunlight, welding)
- sports (protection from contact; protection when swimming or diving)

- eyeglasses (polycarbon lenses for optimal protection against shattering)
- working with power tools
- exposure to environment with high airborne pollutants (such as sawdust)

Though regular eyeglasses and sunglasses provide some protection against injury, they do not provide adequate protection when working with power tools, during recreational and athletic activities, and for specialized needs (such as welding).

Regular Ophthalmic Examinations

In the United States, basic screening for eye problems takes place shortly following birth (for infants born in hospitals and birthing centers), at regular well-child check-ups, through public school vision screening programs, and as part of the ROUTINE MEDICAL EXAMINATION. People who have normal vision require only ophthalmic examinations, the need for which becomes more frequent with advancing age as the likelihood of health conditions that affect vision increases with age. People who have eye conditions, REFRACTIVE ERRORS, HYPERTENSION, DIABETES, and other chronic health conditions need regular ophthalmic examinations as their physicians or eye care providers recommend.

See also CORRECTIVE LENSES; OPHTHALMIC EXAMINATION; VISION IMPAIRMENT.

vision impairment The uncorrectable loss of vision. About 12 million Americans have vision impairments that prevent them from participating in occupations and activities that have requirements or legal standards for VISUAL ACUITY (the ability to see clearly) and VISUAL FIELD (the scope of peripheral vision). People who have functional vision, also called low vision, generally have visual acuity correctable to between 20/40 and 20/400. More than a million Americans are legally blind. Vision impairment may be temporary or permanent.

LEGAL BLINDNESS

VISUAL ACUITY uncorrectable to 20/200 in the better eye, or
VISUAL FIELD uncorrectable to greater than 20 degrees

Symptoms and Diagnostic Path

In children, the symptoms of vision impairment may be difficult to detect. Those that are obvious include

- STRABISMUS, which indicates AMBLYOPIA
- squinting
- holding objects very close to the face
- sitting very close to the television
- frequent headaches

Routine screening for EYE and VISION HEALTH takes place at birth (for infants born in hospitals and birthing centers), during routine well-child visits, and through school vision screening programs. The diagnostic path for children in whom screenings detect potential vision problems includes a complete OPHTHALMIC EXAMINATION with testing for visual acuity, REFRACTIVE ERRORS, and visual field as the child's needs require. Eye care specialists use assessment methods appropriate for

RECOMMENDED ROUTINE EYE EXAMS

Age	Eye Exam Frequency
Birth to 2 years	screening at well-child visits
3 to 5 years	screening every one to two years at well-child visits
6 to 19 years	screening at routine medical exam; ophthalmic exam as needed
20 to 29 years	ophthalmic exam once during this time
30 to 39 years	ophthalmic exam every five years
40 to 65 years	ophthalmic exam every two years
65 years and older	ophthalmic exam every year

the child's age, comprehension, and communication abilities.

Sudden loss of vision in one eye or both eyes is an emergency that requires immediate medical care.

Adults are generally able to perceive symptoms of vision impairment, though when onset is gradual the symptoms are less obvious (though may be more apparent to co-workers, friends, and family members). Sometimes the first indication of a serious vision impairment comes with a misfortune such as a motor vehicle accident, especially among older adults who do not notice or do not acknowledge diminishing vision. Symptoms of vision impairment include

- dimness or changes in color perception
- need to hold objects closer or farther away from eyes
- frequent headaches or squinting
- loss of sharpness or clarity of vision
- difficulty reading
- difficulty seeing at night or in low light
- the need for bright lighting

The diagnostic path includes a comprehensive ophthalmic examination to assess visual acuity, visual field, and refractive error as symptoms indicate. Further diagnostic procedures may be necessary when the underlying cause of vision impairment appears to be a health condition other than a problem with the eyes, such as MULTIPLE SCLEROSIS or DIABETES.

COMMON CAUSES OF VISION IMPAIRMENT

AGE-RELATED MACULAR DEGENERATION (ARMD)	ALBINISM
AMBLYOPIA	CATARACT
central serous RETINOPATHY	congenital CYTOMEGALOVIRUS (CMV)
congenital disorders	corneal deterioration
GENETIC DISORDERS	GLAUCOMA
INFECTION	MULTIPLE SCLEROSIS
RETINAL DETACHMENT	RETINOBLASTOMA
retinopathy of DIABETES	retinopathy of HYPERTENSION
retinopathy of prematurity	STROKE
TRAUMA TO THE EYE	uncorrectable MYOPIA

Treatment Options and Outlook

Treatment depends on the cause of the VISION IMPAIRMENT. CORRECTIVE LENSES or REFRACTIVE SURGERY typically improve vision in conditions such as severe MYOPIA or ASTIGMATISM, even if these measures cannot fully restore normal vision. Surgery is often the solution for vision impairment due to CATARACT, CORNEAL INJURY or deterioration, RETINAL DETACHMENT, and some forms of GLAUCOMA. Medications can control other forms of glaucoma.

Vision impairment has a significant effect on QUALITY OF LIFE. There are numerous assistive devices for people who have functional limitations as a result of vision impairment. Most people who have vision impairments are able to participate, with reasonable accommodations and sometimes creative effort, in work and recreational activities they enjoy. Continued advances in technology generate new treatment approaches that may offer improved vision.

Risk Factors and Preventive Measures

Many health conditions can contribute to or cause vision impairment. The most significant are diabetes, HYPERTENSION, and glaucoma. Early diagnosis and appropriate treatment can limit or prevent damage to the eyes and to vision. Eye protection, such as sunglasses and safety eyewear for activities with risk for impact or debris, is a key preventive measure. More than 40,000 preventable eye injuries occur every year. Routine ophthalmic examinations detect eye problems early, allowing for the most appropriate and effective interventions to preserve vision.

See also BRAILLE; COLOR DEFICIENCY; HEADACHE; MOTOR VEHICLE ADDIDENTS; VISION HEALTH.

vitrectomy An OPERATION to remove the vitreous humor from within the EYE as treatment for RETINAL DETACHMENT, vitreous HEMORRHAGE (bleeding into the vitreous humor), RETINOPATHY, and foreign body penetration. In vitrectomy, the ophthalmologist makes three tiny incisions in the sclera (white portion) of the eye for the insertion of a cutting instrument, a light, and an infusion tube. The cutting instrument rotates to gently pull the vitreous humor out of the eye, and the ophthalmologist replaces it with a saline-based solution at the same rate to maintain pressure and stability within the

eye. Recovery from uncomplicated vitrectomy takes about two to three weeks. Complex vitrectomy, such as when there is retinal detachment or a macular tear, may require additional methods to help the eye heal. Recovery from complex vitrectomy may take several months, though usually preserves vision and the eye.

See also AGE-RELATED MACULAR DEGENERATION; CATARACT EXTRACTION AND LENS REPLACEMENT; CORNEA TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

vitreous detachment The separation of the vitreous humor, the gelatinous substance within the EYE, from the RETINA. Vitreous detachment commonly occurs with advancing age as the vitreous humor thins and takes on more of a liquid consistency. By itself vitreous detachment is harmless and has no effect on vision, though it typically produces FLOATERS (fragments of tissue that float through the vitreous humor). Vitreous detachment with accompanying flashes of light or large numbers of floaters may indicate RETINAL DETACHMENT, an ophthalmologic emergency that requires immediate treatment.

See also VITRECTOMY.

xanthelasma Deposits of fatty plaque that form blisterlike lesions on the eyelids, usually the upper eyelids near the corner of the NOSE. The lesions are yellowish in color and often indicate HYPERLIPIDEMIA (elevated BLOOD levels of cholesterol and triglycerides). Though harmless, the lesions can cause the eyelid to droop, obscuring vision when an upper lid and interfering with lid closure when a lower lid. A plastic surgeon can remove the lesions in a simple outpatient OPERATION, though the lesions tend to recur, particularly when blood lipid levels remain high.

See also BLEPHAROPLASTY; CHOLESTEROL BLOOD LEVELS; LESION; SURGERY BENEFIT AND RISK ASSESSMENT; TRIGLYCERIDE BLOOD LEVEL.

THE INTEGUMENTARY SYSTEM

The integumentary system encloses the body, protecting it from, as well as allowing its interactions with, the external environment. Physician specialists who treat conditions of the SKIN, HAIR, and NAILS are dermatologists. This section, "The Integumentary System," presents an overview of the structures and functions of the integumentary system, a discussion of dermatological health and disorders, and entries about the health conditions that can affect the skin, hair, and nails.

Structures of the Integumentary System

SKIN
- epidermis
- dermis
- subcutaneous layer

SWEAT GLANDS
- eccrine sweat glands
- apocrine sweat glands

HAIR
- follicle
- shaft

SEBACEOUS GLANDS
- sebaceous
- ducts

NAILS
- cuticle
- nail
- nail bed
- matrix
- (nail root)

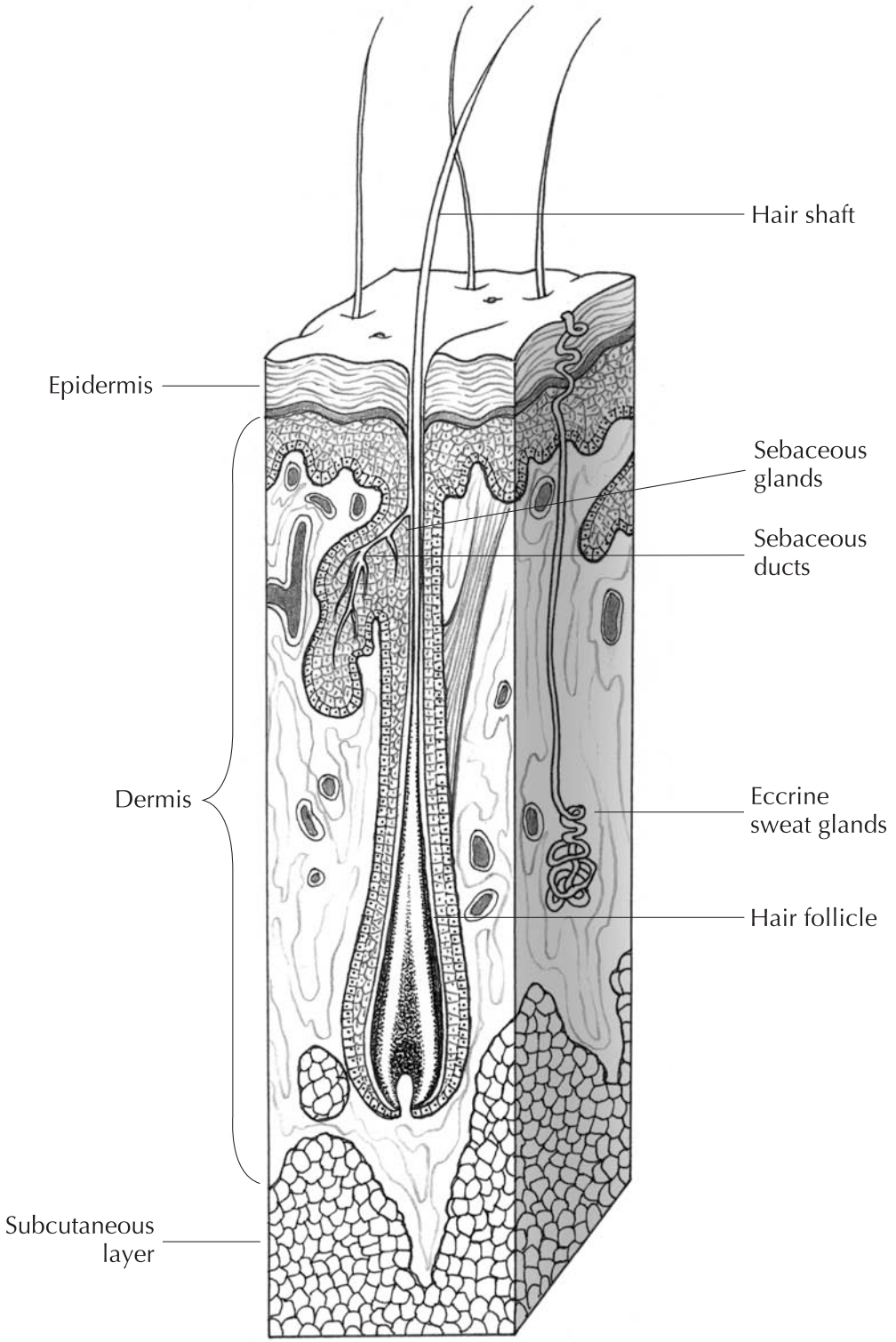
Functions of the Integumentary System

The integument, from the Latin word for "cloak," covers the body. Its structures—the SKIN, HAIR, and NAILS—form the image the body presents to the outside world. Its functions—protective barrier, tactile perception, temperature regulation, IMMUNE RESPONSE—enable the body to survive in that outside world.

The foundation of the integumentary system is the skin, which, as the body's largest organ, accounts for 15 percent of the body's weight. It sheaths the body in protective insulation from scalp to sole, coating every stretch and fold between. The skin's three layers—epidermis, dermis, and subcutaneous layer—form the interface between the body's internal and external environments. The endless exchange of information is so wearing that the skin completely replaces its outermost layer, the epidermis (about 36,000 square inches of surface area), every three to four weeks. What looks remarkably the same from day to day is, in reality, always changing.

In the beginning Attesting to the skin's importance for survival and function, the skin and the BRAIN are the first two distinctive organs to emerge during embryonic development. The cells of each arise from the primitive neural crest, also called the neuroectoderm. By three weeks of gestational age the neural crest differentiates. The cells that migrate inward become NERVE cells, forming the brain and SPINAL CORD. The cells that migrate outward become the two major cell types of cells that form the skin: keratinocytes and melanocytes.

By seven weeks gestational age the skin develops hair follicles that, six weeks later, begin to cover the head with hair. At 20 weeks gestational age that hair coat, called lanugo, has spread to cover the entire body. Some babies, especially those born prematurely, still sport this coat at birth, which is often disconcerting to anxious parents but quickly falls away. The formation and function of the sebaceous glands parallels that of the hair follicles. As hair begins to sprout, the sebaceous glands secrete a thick, ointmentlike precursor to sebum, called vernix, that covers the skin's surface. Vernix establishes a waterproof barrier that protects the skin as the FETUS floats in AMNIOTIC FLUID. Also by 20 weeks the skin contains SWEAT GLANDS, eyelashes and eyebrows, fingernails and toenails, and the unique surface ridges on the fingertips that will become fingerprints.


Hair shaft
Epidermis
Sebaceous glands
Sebaceous ducts
Dermis
Eccrine sweat glands
Hair follicle
Subcutaneous layer

Renewal and protection: the epidermis The primary cells of the skin's surface layer, the epidermis, are melanocytes, which produce the pigment melanin, and keratinocytes, which produce the fibrous protein keratin. Both types of cells arise from the base level of the epidermis, the stratum germinativum ("birth"), also called the basal level or the Malpighian level. As the Latin name implies, this level germinates, or originates, cells. Melanocytes remain in the stratum germinativum for all of their existence. Keratinocytes migrate upward to the stratum corneum ("horny"), the cornified or hardened surface level of the epidermis.

Melanocytes produce melanin, the pigment that gives color to the skin, hair, and eyes (iris). This color has a purpose: melanin is the skin's primary protection against the sun's ultraviolet rays. It absorbs ultraviolet lightwaves, preventing them from causing damage to cell structure and function. Melanocytes store the enzyme tyrosinase, which other cells in the body produce, and acquire the amino acid tyrosine from the circulating blood. The tyrosinase catalyzes a series of chemical actions that convert tyrosine to two tones of pigment: eumelanin (black-brown pigment) and pheomelanin (yellow-brown pigment). The melanocytes package these pigments into granules collectively called melanin.

Melanocytes also pigment cells in other organs. When the neural crest differentiates early in embryonic development, some melanocytes migrate with the cells that form the structures of the brain. A dense population of melanocytes settles in a structure in the midbrain, the substantia nigra (a name that means "black substance"). The melanocytes pigment specialized cells in the substantia nigra that produce DOPAMINE, a brain NEUROTRANSMITTER essential to neuromuscular function. When melanocytes in the skin slow melanin production, the result may be depigmentation disorders such as VITILIGO or white hair. Though often distressing, these consequences are not serious threats to health and life. When melanocytes in the substantia nigra stop producing melanin, however, the substantia nigra stops producing dopamine, and the body stops moving, a degenerative condition called PARKINSON'S DISEASE.

Keratinocytes produce two proteins: keratin, a fibrous substance, and cytokine, an IMMUNE RESPONSE mediator. After they mature in the stratum germinativum, keratinocytes pick up melanin granules and begin their migration to the surface. The three and a half week journey to the stratus corneum is a final rite of passage that literally squeezes the life from the keratinocytes. During this passage, the keratinocytes undergo denuclearization, a process of nucleus deterioration that gradually diminishes cell function. The upswell of continuous movement that carries the keratinocytes along compresses their remaining cell structure. By the time the keratinocytes break through to the surface, they are flat, brittle, and lifeless husks of keratin. They layer tightly against one another, forming the tough covering the skin presents to the outside world. The friction of interacting with the external environment brushes them loose and they fall away, a process called exfoliation. Keratinocytes that funnel through the hair follicles become hair shafts.

WHY A WOUND THAT FAILS TO HEAL MAY SUGGEST SKIN CANCER

The epidermis completes a total turnover of cells every 24 to 28 days, meaning that this outer layer of the SKIN is fresh and new about once a month. Any skin wound that takes longer than three or four weeks to heal represents an area of cells that is growing at its own pace, distinct from the other skin cells—in short, a CANCER.

Structure, sustenance, and sense: the dermis The skin's middle layer, the dermis, nurtures and supports the skin. Primarily fibrinogens create a collagen matrix that supports an abundant and effusive network of blood vessels, nerves, and glands (sweat and sebaceous). These structures are elemental to the body's heat regulation mechanisms. The dermis also contains the Langerhans cells, the gatekeepers of the SKIN-ASSOCIATED LYMPHOID TISSUE (SALT) that are the front line of the body's immune response.

The tiny blood vessels—arterioles and venules—that web through the dermis cause the skin to flush when the body is too warm. This function of heat regulation uses the BLOOD vessels for conduction heat dispersal, dilating them to bring a flood of blood to the cooler temperatures near the surface. The vessels contract when body temperature returns to an acceptable range, send-

ing the blood back within the body's core. This same mechanism also responds to strong emotions such as fear or embarrassment, similarly sending blood rushing to the skin. The blood supply of the dermis also nourishes the epidermis, supporting the perpetual production of new cells in the stratum germinativum.

About 5 million sweat glands aid both temperature and fluid regulation, dripping out about 500 milliliters of somewhat salty water every hour. Most of this moisture evaporates without conscious awareness of its presence. Sweating becomes an obvious event only when it becomes profuse, as with intense exercise or heat, or in conditions such as HYPERHIDROSIS. The eccrine sweat glands secrete their fluid directly to the surface of the skin through sweat pores. The apocrine sweat glands, found primarily in the axillae (underarms) and groin areas, secrete their fluids into the hair follicles. Sweat from the eccrine glands is water and electrolytes (salts), while that from the apocrine glands contains lipids and proteins to help it mix with the sebum in the hair follicles. These extra substances account for the familiar odor of sweat as well as the yellowish stains sweating leaves in the underarm areas of clothing.

THE SUNLIGHT VITAMIN

Though the negative consequences of ultraviolet light get the most press, sunlight is a valuable resource for strong bones and TEETH. The dermis contains ergosterol, a chemical that ultraviolet light converts into vitamin D, which the body needs to use calcium to build BONE and tooth enamel.

Millions of specialized nerve endings reside within the dermis, gathering data about temperature, humidity, motion, and contact, which they transmit to the NERVOUS SYSTEM. The skin is the organ of tactile perception, the sense of touch. The highest concentrations of tactile receptors are in the fingertips, the lowest on the soles of the feet. The key structures that detect touch are the discs of Merckel (light touch) and the corpuscles of Meissner (moderate touch), specialized nerve endings that transmit impulses to specially dedicated regions of the cerebral cortex that interpret the nerve messages and initiate the appropriate responses. The structures that detect heavier pressure, the corpuscles of Ruffini and the Pacinian corpuscles, reside deeper in the dermis, near or extending beyond the subcutaneous border.

Cushion and connection: the subcutaneous layer The subcutaneous layer, also called the hypodermis, contains mostly adipose tissue (body fat) and some connective tissue. The adipose tissue warehouses the excess calories the body converts to fat, varying in thickness to accommodate this stored energy source. A rich network of blood vessels and nerves permeates the subcutaneous layer, supplying nourishment to all layers of the skin and conducting nerve impulses from sensory receptors and other nerve structures. The subcutaneous layer gives shape and context to the skin, softening the protrusions and angles of the underlying musculoskeletal structures. It also cushions those underlying structures from the multitude of minor traumas the body's surface experiences every day.

The connective tissue of this deepest layer of the skin binds the upper skin layers to the internal structures of the body, overlaying the muscles. Fibers of connective tissue lace from the subcutaneous layer upward into the epidermis and downward to the musculoskeletal structures, holding the skin in place. These connections allow the skin to respond to the movement of muscles beneath it. In locations such as the knuckles, the connections are loose (appearing deeply creased) to accommodate substantial motion. In the face, by contrast, the skin tethers tightly to the underlying structures. When the facial muscles move the skin on the face moves, too, forming facial expressions.

The hair Hair has different characteristics and functions, depending on its location on the body. Though in many other mammals hair may serve for protection and heat regulation, in humans hair has mostly lost these purposes. The exceptions are the hair on the head and a man's unshaven beard, which help preserve heat and shelter the skin from sunburn. Hair in other locations has specific functions. Hair in the auditory canal and in the nasal passages helps move debris to the outside of the EAR and NOSE, respectively. The eyebrows keep sweat from running into the eyes, and the eyelashes help prevent environmental debris such as dust or pollen particles from entering the eyes.

Deep at the base of the hair follicle within the dermis (middle layer of the skin) is the hair root, which forms the cells that will become the hair fiber. At their formation, hair cells are pliable, living, and colorless. The new cells that emerge from the root divide, pushing the cells that preceded them upward into the hair follicle. As the cells rise, they move beyond the range of the blood vessels that bring nourishment to the hair root and so die.

By the time hair cells rise above the surface of the skin, they are hard and compressed into an elongated, two-layer fiber. The inner layer, the cortex, is about three or four cells thick, composed of melanocytes and keratinocytes. Melanocytes form the melanin (pigment) that gives hair its color and. Large, numerous melanocytes result in black or brown hair; small, scattered melanocytes result in red or blond hair. A reduction in the number of melanocytes results in gray or white hair. The keratinocytes produce the keratin that gives hair its structure. A single layer of cells, the cuticle, encases the cortex. The rounder the hair fiber, the straighter the hair. Curly or kinky hair fibers are flat.

A hair follicle on the scalp typically grows hair for three to five years, then enters a period of dormancy that lasts a few months after which time it drops the hair and the growth cycle begins anew. Some people can grow hair for longer, up to seven or eight years, while others have a shorter growth period. The amount of time hair grows influences though does not regulate the hair's length; a person with a short growth period can have hair that grows rapidly.

Between 10 and 20 percent of the body's hair follicles are dormant at any one time. Hair follicles elsewhere on the body have shorter growth cycles than those on the head. The hairs of the eyebrows regenerate every 100 days or so, for example. An individual's genetic composition determines the shape, color, and length of hair fibers. The cells of the hair fibers within most of the hair follicle and visible above the skin's surface are dead and do not require nourishment or have sensory capability. Their keratin content and cuticle layer keeps them attached to the body.

Fingernails and toenails Keratin also gives the fingernails and toenails their shape and hardness. The nails cover the top portion of the fingers and toes. Though they may appear to have little more function than to serve as decorative platforms, the nails give the fingers (and to more limited extent, the toes) the ability to grip, pry, and scratch. The nails also give firmness and STRENGTH to the ends of the fingers, and help protect the sensitive fingertips.

Health and Disorders of the Integumentary System

The skin performs its myriad functions with remarkable consistency. Because it replaces its outer layer every three to four weeks, the skin remains relatively healthy for most of the lifespan. However, well over a thousand disorders, diseases, and conditions can affect the skin, hair, and nails. While a few can cause permanent tissue damage or even death, most are fairly benign.

Traditions in Medical History

For millennia the internal structures of the body mystified and confounded healers and physicians. The skin, however, was right there on the outside of the body for all to see and touch. The skin's accessibility gave it a perceived, and erroneous, simplicity as nothing more than the body's covering. Not until the electron microscope made it possible to explore the molecular structures of the body did scientists begin to understand the true complexity and intricate functions of the skin.

Today doctors recognize that the skin is a complex and multifunctional organ. Its appearance reveals much about the body's internal functions and a person's health status. Numerous systemic health conditions reveal or manifest themselves through changes in the skin, hair, and nails. Discoloration of the skin, for example, may suggest SUNBURN (red), JAUNDICE and LIVER disease (yellow), or cardiovascular or pulmonary disease (cyanotic blue). Variations on discoloration accompany numerous rashes. The characteristics of skin eruptions are often unique to specific diseases, such as the pustules of CHICKENPOX and the papules of MEASLES. Disturbances of the fingernails and toenails may similarly portend underlying health conditions such as iron-deficiency ANEMIA (koilonychia or spooning) or EMPHYSEMA (yellow nail syndrome). And hair loss, always emotionally distressing, may be a harbinger of undiagnosed thyroid disease or toxic exposure.

CONDITIONS THAT CAN AFFECT THE INTEGUMENTARY SYSTEM

ACNE	ACROCHORDON	ACTINIC KERATOSIS
ALBINISM	ALOPECIA	ANGIOMA
BURNS	CANDIDIASIS	CARBUNCLE
CELLULITIS	CHLOASMA	DISCOID LUPUS ERYTHEMATOSUS
CORNS	CRADLE CAP	DANDRUFF
DECUBITUS ULCER	DERMATITIS	DERMATOFIBROMA
DIAPER RASH	ECCHYMOSIS	ERYSIPELAS
erythema	ERYTHRASMA	FOLLICULITIS
FROSTBITE	FURUNCLE	HYPERHIDROSIS
IMPETIGO	KAPOSI'S SARCOMA	KERATOACANTHOMA
KERATOSIS PILARIS	LENTIGINES	LICHEN PLANUS
LICHEN SIMPLEX CHRONICUS	LIPOMA	malignant melanoma
MILIARIA	ONYCHOMYCOSIS	PEDICULOSIS
PEMPHIGUS	PRURIGO	PRURITIS
PSORIASIS	PSUEDOFOLLICULITIS BARBAE	PURPURA
RASH	ringworm	ROSACEA
scleroderma	SKIN CANCER	SUNBURN
TELANGIECTASIS	TINEA	TOXIC EPIDERMAL NECROLYSIS
VITILIGO	warts	XANTHOMA

Breakthrough Research and Treatment Advances

Among the most exciting advances in dermatology are new techniques in SKIN REPLACEMENT and new laser technologies, which vastly extend treatment options for a wide spectrum of health conditions involving the skin. Skin replacement techniques such as synthetic skin and tissue expansion promise new hope for reconstruction following severe BURNS, trauma, and CANCER surgery. Refinements in laser technology allow dermatologists and surgeons to finely pinpoint potentially damaging or deadly cancer cells to eradicate them without destroying adjacent tissues. Lasers also offer potential relief from severe, disfiguring dermatologic conditions such as PSORIASIS and ACNE. As well, knowledge emerging from HUMAN GENOME mapping is helping researchers identify the causes of persistent or debilitating conditions such as vitiligo and PEMPHIGUS.

Among the greatest successes in modern medicine is the virtual elimination of skin cancer as a threat to life. Basal cell carcinoma and squamous cell carcinoma, the most common skin cancers, are nearly 100 percent curable with early detection and treatment. Dermatologists diagnose these cancers in 1 million Americans each year. Health experts attribute the success in reducing serious consequences and death from these cancers to nearly nil to the combination of effective sunscreens to prevent the sun damage that causes these skin cancers and improved techniques for detecting and removing cancerous and precancerous lesions.

The rapid and continual regeneration of the epidermis intrigues researchers, who continue to explore the molecular foundations of this function. Some scientists believe that there are correlations between KERATINOCYTE replication and stem cells that could hold important clues to understanding what determines how a cell becomes specialized for certain functions. Stem cells have the unique ability to differentiate, or become various kinds of particular cells, depending on the stimulation they receive. Researchers involved in this line of investigation are hoping to find ways to redirect keratinocytes to form other kinds of cells, which has exciting implications for guiding the body to heal itself by growing healthy tissues to repair or replace diseased organs and structures.

A

acne INFLAMMATION of the SKIN's sebaceous structures, also called acne vulgaris, that results in eruptions on the skin surface commonly called pimples, whiteheads, and blackheads. Acne occurs when excessive sebum traps BACTERIA and skin cells, clogging the follicles. The clogged follicles provide an ideal incubator for the bacteria *Propionibacterium acne,* which is normally present on the surface of the skin where continuous exposure to the air keeps it in check. Within the airless environment of a clogged hair follicle, however, these anaerobic bacteria, which do not require oxygen, thrive.

Acne is most common in PUBERTY and is a consequence, most doctors believe, of the natural surge in sex HORMONE production, notably TESTOSTERONE, that heralds the onset of puberty. Testosterone stimulates the sebaceous glands surrounding the HAIR follicles, increasing their production of sebum, a thick, oily substance that helps lubricate the skin. Women experience hormonal changes during MENSTRUATION, PREGNANCY, and MENOPAUSE that may cause acne outbreaks, because estrogen suppresses sebum production. Newborn infants may develop acne during the first few weeks of life, a reaction to the surge of hormones the infant receives from his or her mother in the few days before birth. Contrary to popular belief, foods high in fats or sugars, such as french fries or donuts, have little if any influence on acne. However, cosmetics and oily products applied to the skin that block the sebaceous structures can contribute to or aggravate acne outbreaks.

Acne commonly erupts on the face, upper back, and chest as these areas contain large numbers of hair follicles. Acne seldom affects scalp follicles. An outbreak begins as small, reddened bumps, called comedones or papules, that may hurt or itch. As the sebaceous structures become more inflamed, the bumps enlarge into closed (whiteheads) or open (blackheads) lesions. Lesions that form near the surface of the follicles are pimples; those that expand below the surface of the skin are nodules or cysts. The most serious form of acne is nodulocystic acne, in which numerous nodules and cysts form deep within the follicles though inflammation that extends above the skin's surface. Nodulocystic acne typically leaves scars or pits after the lesions heal, and may extensively damage the skin.

Symptoms and Diagnostic Path

The symptoms of acne are its characteristic bumps and lesions, making diagnosis fairly straightforward. Doctors diagnose acne on the basis of its appearance and the hormonal stages the individual may be going through. Acne that does not fit the characteristic presentation may be a symptom of an endocrine disorder that allows elevated testosterone levels, such as POLYCYSTIC OVARY SYNDROME (PCOS) or CUSHING'S SYNDROME. Laboratory tests to measure hormone levels can assess this possibility. Rarely, the doctor may choose to BIOPSY several lesions to confirm the diagnosis.

Treatment Options and Outlook

Treatment for acne targets reducing inflammation, sebum production and accumulation, and the presence of infective agents such as *P. acne*. Products may be topical (applied to the affected areas of the skin for localized effect) or systemic (medications taken by mouth for generalized effect). *P. acne* tends to develop resistance to antimicrobial products over time, making it necessary to switch among medications for optimal effectiveness. Acne is self-limiting and will improve over time without treatment, though severe acne may leave

scars. Products to treat mild to moderate acne are available without a doctor's prescription. Prescription-only medications, such as topical and oral antibiotics, are necessary for moderate to severe acne. Most people use several kinds of products concurrently.

Over-the-counter products and self-care Products available without a doctor's prescription to treat acne generally contain astringents, exfoliants, and antimicrobials, sometimes in combination with one another. The common product Clearasil, for example, combines resorcinol, which slows the production of keratocytes, and sulfur, an antimicrobial. Such products cleanse excess oils, debris, and dead cells from the skin. Antiseptic or antimicrobial substances help suppress *P. acne* and other bacteria normally present on the skin, reducing the potential for INFECTION and inflammation.

COMMON INGREDIENTS IN OVER-THE-COUNTER ACNE PRODUCTS

Product	Actions
acetone	astringent
ALCOHOL	antimicrobial
benzoyl peroxide	antimicrobial, exfoliant
lactic acid	exfoliant, mild antimicrobial
resorcinol	exfoliant
salicylic acid	exfoliant, astringent
sulfur	antimicrobial

Prescription medications The two general categories of medications doctors prescribe for acne are antibiotics and retinoids, in topical and oral forms. ANTIBIOTIC MEDICATIONS target bacteria such as *P. acne*. Oral antibiotic therapy may extend over six months or longer, at doses lower than those typically prescribed to treat acute infections.

Isotretinoin causes BIRTH DEFECTS. Current practice standards require two negative PREGNANCY tests and use of reliable CONTRACEPTION (such as oral contraceptives) before dermatologists may prescribe isotretinoin therapy for women of childbearing age.

In people who have severe or pitting acne, treatment with oral isotretinoin nearly always ends further acne outbreaks because the isotretinoin permanently alters the structure and function of the sebaceous structures. However, oral isotretinoin has numerous, and potentially serious, side effects that make it a treatment option when other methods have failed to control the acne. All of the retinoids can cause BIRTH DEFECTS; women who are or could become pregnant should not use these medications. Oral contraceptives (birth control pills) often improve acne that follows the MENSTRUAL CYCLE.

COMMONLY PRESCRIBED MEDICATIONS FOR ACNE

Antibiotics	
erythromycin (topical and oral)	minocycline (oral)
tetracycline (topical and oral)	doxycycline (oral)
sulfacetamide (topical)	
Retinoids	
isotretinoin (topical and oral)	tretinoin (topical)
adapalene (topical)	tazarotene (topical)

Outlook Acne is self-limiting. Most acne ceases when the body's hormone levels stabilize. For adolescents, this occurs at the culmination of puberty, generally by the late teens (females) or early twenties (males). In women, acne outbreaks may occur regularly with the menstrual cycle. Acne related to the hormonal changes of pregnancy generally goes away within three months of childbirth. Acne is uncommon in postmenopausal women.

Risk Factors and Preventive Measures

Because acne results from a convergence of factors, key among them hormonal shifts in the body, there are no known measures for preventing its occurrence. Many myths have prevailed through the years about the relationship between foods and acne. Though nutritious eating habits are important for overall health and development as well as the skin's general health, foods do not influence the course or severity of acne. Similarly, though poor hygiene contributes to numerous problems with the skin and may exacerbate acne by encouraging the growth of bacteria, it does not in itself cause acne.

Diligent daily hygiene, such as gentle cleansing with an antibacterial soap, helps prevent acne lesions from becoming infected. Zealous washing

and scrubbing can aggravate acne, causing increased inflammation and irritation. Harsh soaps that dry the skin may temporarily reduce surface oils but can cause flaking and other problems. Using an astringent according to the doctor's instructions can draw excess oils from the sebaceous structures without so much irritation to the surrounding skin. Dermatologists often recommend lubricating lotions and creams that do not block the pores to help maintain the skin's moisture.

See also DERMATITIS; FOLLICULITIS; KERATOCYTE; LESION; MILIARIA; NODULE; PAPULE; ROSACEA; SEBACEOUS GLAND.

acrochordon A polyp that commonly grows externally from SKIN folds, such as those around the eyelids and on the neck, underarms, and groin. Also called a skin tag or fibroepithelial polyp, an acrochordon is noncancerous and harmless (benign). Doctors do not know what causes acrochordons to develop. Some acrochordons contain one of the HUMAN PAPILLOMAVIRUS (HPV) strains, though others do not. Acrochordons become more common with advanced age, and are most likely to appear in people who are between the ages of 50 and 75. Unlike intestinal polyps, acrochordons do not become cancerous. The dermatologist may remove an acrochordon that is in a location of frequent irritation or cosmetically unacceptable.

See also INTESTINAL POLYP; PLASTIC SURGERY.

actinic keratosis Precancerous growths (lesions) on the SKIN, also called solar keratosis, that develop as a consequence of damage from overexposure to the sun. Actinic keratosis becomes more common with advancing age. Lesions are most common on the face, scalp, chest, hands, and arms though can develop anywhere on the body that receive extensive sun exposure. In their early stages, the lesions appear scaly and rough, and bleed easily. In later stages, the lesions acquire a wartlike appearance. Most squamous cell SKIN CANCER arises from actinic keratosis. Removing the lesions prevents them from developing into CANCER. Between 10 and 20 percent of untreated actinic keratosis develops into squamous cell skin cancer, though it is not possible to determine which lesions will remain benign and which will turn cancerous.

Symptoms and Diagnostic Path

The lesions of actinic keratosis follow a typical and consistent progression of symptoms. Actinic keratosis begins with a small, scaly patch of skin that may itch. It often appears to heal or peel off, then recurs. The LESION may be grayish, may reddened (erythematous), or may be the same color as the skin. Most people first feel rather than see the lesion. As changes to the skin cells at the site continue, the lesion becomes more defined and apparent. The lesion may resemble a wart, or may become hardened and overgrown, developing a tough, thick texture (hyperkeratosis).

Because the progression of actinic keratosis is so characteristic, the dermatologist generally makes the diagnosis on the basis of appearance and history of sun exposure. The dermatologist may choose to biopsy larger or suspicious lesions to determine whether they have progressed to squamous cell skin cancer. Unless such suspicion exists, there is no need for biopsy because the standard treatment is to remove the lesion, which consequently eliminates the lesion's risk for evolving into a cancer.

Treatment Options and Outlook

Treatment for actinic keratosis is removal of existing lesions coupled with regular (every 6 to 12 months) examinations of the skin to detect new lesions. Methods for removing the lesions include

- cryotherapy, such as liquid nitrogen, which freezes the lesion, causing the cells to die and slough away
- electrocautery, which burns away the lesion
- curettage, in which the dermatologist scrapes off the lesion using a sharp surgical blade
- topical application of a chemotherapy agent, which causes the cells in the lesion to die and slough away
- photodynamic therapy, in which the dermatologist applies a photosensitive chemical that accumulates in the affected cells and then administers certain frequencies of light exposure that cause the cells containing the photosensitive chemical to die

Treatment may cause discomfort. Small lesions typically heal in two to three weeks with minimal or no scarring. Larger or numerous lesions may result in pitting and scarring that will require subsequent cosmetic treatment. Though removal ends the threat of squamous cell skin cancer from existing lesions, the likelihood is high that new lesions will develop. Dermatologists recommend annual or semiannual skin examinations for people who have had actinic keratosis lesions removed.

Risk Factors and Preventive Measures

Actinic keratosis develops only in people who have repeated or severe exposure to the sun or other sources of ultraviolet radiation such as tanning booths. It reflects longstanding damage, typically that occurred in childhood or over decades of sun exposure in adulthood. The lesions emerge and progress over years and are most common in people age 50 and older.

People who are likely to develop actinic keratosis are those who:

- experienced severe SUNBURN as children (blistering and peeling)
- are fair skinned and do not tan easily
- work outdoors
- engage in outdoor activities such as gardening and sailing that result in prolonged sun exposure
- live in areas where sun intensity is high, such as the southern United States

Preventive measures include avoiding outdoor activities during the highest intensity of sunlight (typically 10 a.m. to 3 p.m. daily) whenever possible, and diligent SUN PROTECTION when outdoors during daylight hours. Dermatologists recommend wearing a full-brimmed hat and long sleeves when extended sun exposure is unavoidable and applying sunscreen to the face, backs of the hands, and other skin surfaces that remain exposed. Sunscreen should have a sun protection factor (SPF) rating of 15 or higher and protect against both ultraviolet A (UVA) and ultraviolet B (UVB).

See also LENTIGINES; SKIN SELF-EXAMINATION.

age spots See LENTIGINES.

aging, integumentary changes that occur with Though the premise of aging tends to conjure images of WRINKLES and gray HAIR or baldness, the SKIN, hair, and NAILS undergo numerous changes across the lifespan.

Integumentary Changes in Youth

During infancy and early childhood, the integumentary structures are soft and the hair may be fine. By about age 10 or 11 years, the hormonal shifts of PUBERTY are under way. Isolated pimples may break out on the face, chest, and back. Hair patterns begin to change as the sex hormones stimulate SECONDARY SEXUAL CHARACTERISTICS such as axillary (underarm) and pubic hair growth. Within a few years the hair on the legs thickens and darkens, and boys begin to sprout facial hair. The sebaceous structures kick up sebum production, and the dermis accelerates cell production to accommodate new skin to cover what can amount to several inches of new height each year. ACNE, an inflammatory process involving the sebaceous structures, is the most common skin condition that occurs between the ages of 14 and 22.

The skin, hair, and nails outwardly remain relatively stable during young adulthood, the third and fourth decades of life, though are collecting the cumulative effects of factors such as sun exposure, scarring, and other evidence of life experience. People who work outdoors or participate in outdoor activities begin to show these effects earlier than their counterparts who limit their exposure the natural elements. Repeated sun exposure may result in tanning, a look that may be fashionably desirable though also causes LENTIGINES (freckles and "age" spots), roughness, and wrinkles. The hands may develop calluses and the feet CORNS.

Integumentary Changes in Midlife

At about age 40 the connective tissues throughout the body begin to gradually lose elasticity, allowing the skin to sag and form more wrinkles. Dermatologists call this loss elastosis. As well, the epidermis (outer layer of the skin) and the adipose tissue (fat) beneath the skin both thin. The epidermis becomes more fragile and susceptible to punctures and tears. Though losing a little fat under the skin might sound like a benefit when other areas of the body are demonstrating an age-related propen-

sity to accumulate fat, the diminished integumentary adipose tissue reduces the skin's ability to regulate heat loss and retention. The older people get, the greater their tendency to feel cold even when the external environment is warm. The risk for heat and cold injuries affecting the skin, such as sunburn and frostbite, also increases.

By midlife even the skin of those who are not the outdoors types usually has weathered significant exposure to sun, wind, and chemicals that can cause trauma and damage. ACTINIC KERATOSIS, a condition of precancerous growths on sun-exposed skin, and SKIN CANCER such as basal cell carcinoma or squamous cell carcinoma, may manifest, arising from skin damage that occurred decades earlier. Sunscreen, the mainstay of SUN PROTECTION for children today, had not yet been developed during the childhoods of those who are today over age 30.

Age-related changes begin to affect the hair in midlife, too. Melanocytes, skin cells that produce melanin, thin from the hair follicles, diminishing the amount of pigment that appears in new hair fibers. Reduced pigment produces hair that appears gray; complete absence of pigment produces white hair. These changes occur regardless of the hair's natural hair color. Men and women both experience patterned ALOPECIA (hair loss), though in men the loss of hair is generally more pronounced.

Integumentary Changes in Late Life

By the seventh, eighth, and ninth decades of life, the epidermis becomes so thin as to reveal the coloration of the tissues that lie beneath the skin. The skin drapes loosely over the body, tearing and bruising easily. Blood vessels ridge beneath the skin like pipe cleaners under wet tissue paper, trailing along the backs of the hands and arms and on the lower legs and feet. Threadlike networks of capillaries etch across the cheeks. Late in life, the skin continues to do a remarkable job protecting the body, yet is especially vulnerable to damage.

Maintaining Healthy Skin Across the Lifespan

Anti-aging remedies abound, and some—such as those that add moisture and vitamins to the skin—help the skin remain supple and smooth longer in life than without their use. But the most effective anti-aging approach is to take good care of the skin all through life, beginning in childhood. Appropriate nutrition, protection from the sun and other elements of weather, and good hygiene are simple, yet effective, measures to keep the skin healthy throughout life.

See also CALLUS; FITZPATRICK SKIN TYPE; MELANOCYTE; SCAR.

albinism A genetic disorder in which the melanocytes do not produce, or produce reduced amounts of, melanin, the chemical that deposits pigment in cells of the SKIN, HAIR, and structures of the EYE. Without melanin, the skin, eyes, and hair have little or no pigment and consequently lack color. People who have albinism typically have light to white skin and hair, and light or no color to the irises of the eyes (the pigmented rings around the center of the eyes). Albinism reduces or eliminates the skin's ability to protect itself from exposure to ultraviolet light, greatly increasing the risk for damage such as SUNBURN and SKIN CANCER.

The lack of pigmentation characteristic of albinism extends to the interior of the eye as well, resulting in VISION IMPAIRMENT. In the normal eye the RETINA, the inner lining of the back of the eye that receives light images and encodes them as NERVE signals for the OPTIC NERVE to carry to the BRAIN, is highly pigmented such that it appears black. The pigment suppresses extraneous light and supports the functions of rods and cones, the specialized cells of vision that line the retina. Without the protection of pigment, unfocused lightwaves bombard the retina. The brain cannot sort the resulting nerve signals into images and consequently fails to properly establish the neurologic pathways that make vision (the interpretation of patterns of light as images) possible.

There are a number of INHERITANCE PATTERNS for albinism, nearly all of which are recessive (require a defective pigmentation GENE from each parent). Researchers have identified several types of gene mutations that cause most forms of albinism.

Oculocutaneous albinism (OCA) The three types of OCA involve the skin, hair, and eyes to varying degrees.

- OCA type 1 results from a MUTATION of the gene that encodes tyrosinase, an enzyme necessary

to convert the essential amino acid tyrosine to melanin. OCA type 1 features nearly complete absence of pigmentation and usually legal blindness (refractive correction can achieve vision no better than 20/200).

- OCA type 2 results from a mutation of the *P* gene, which encodes proteins that participate in pigmentation. OCA type 2 features moderate pigmentation and moderate vision impairment (usually correctable to 20/60).
- OCA type 3 results from a mutation of the *TRP-1* gene, which encodes proteins that have incompletely understood roles in the formation of pigment.

Ocular albinism (OA) Ocular albinism results from an X-linked mutation of an as-yet unidentified gene. People who have OA have normal or minimally affected skin and hair pigmentation but lack pigment in the structures of the eye, resulting in vision impairment.

Other forms of albinism Other forms of albinism are less common or may be part of a larger complex of symptoms. Among them are

- Chédiak-Higashi syndrome (CHS), a variation of OCA in which there are also immune and neurologic dysfunctions
- Hermansky-Pudlak syndrome (HPS), a multisystem disorder that involves PLATELET dysfunction resulting in excessive bleeding, vision impairment, and inappropriate fat storage in tissues throughout the body as well as absence of pigmentation in the skin and hair
- Waardenburg's syndrome, a complex of symptoms involving HEARING LOSS and partial albinism (often a lock of white hair in the front of the head with the rest of the hair normal color); people with this disorder may also have pale blue eyes or different color in each eye

Symptoms and Diagnostic Path

The most obvious symptom of albinism, pale coloration of the skin and hair, is apparent at birth. Light-colored eyes and vision problems such as STRABISMUS (inability of the eyes to focus in unison), NYSTAGMUS (involuntary rapid eye movements), and PHOTOPHOBIA (extreme sensitivity to light) are common and also manifest early in infancy.

The characteristic absence of pigmentation is fairly conclusive for diagnosis of albinism. A thorough OPHTHALMIC EXAMINATION with OPHTHALMOSCOPY reveals the retina's hypopigmentation. A VISUAL ACUITY test demonstrates the degree of vision impairment. GENETIC TESTING can identify the causative gene mutation, which helps define the inheritance pattern.

Treatment Options and Outlook

There are no treatments for albinism itself. CORRECTIVE LENSES and methods to correct strabismus or nystagmus, if present, can improve vision to the extent possible. Many people who have albinism have functional vision, even if they have legal blindness, and can participate in most activities that require basic vision though may not be able to drive.

Albinism, particularly OCA type 1, may limit outdoor activities in areas that receive intense sunlight. The sun presents a risk for sunburn and related damage as well as harm to the eyes. Photophobia nearly always accompanies albinism and can make it difficult to remain in bright light, even wearing sunglasses, for any substantial length of time. People who have albinism should wear protective clothing, sunglasses, hats, and high-SPF sunscreen whenever they are outdoors.

Risk Factors and Preventive Measures

The sole risk factor for albinism is genetic mutation. Doctors recommend genetic testing and counseling for families in which members have albinism. Though there is no treatment for albinism, early diagnosis helps minimize the extent of vision impairment that may result from nystagmus or strabismus. People who have albinism also should undergo frequent screening for skin cancer, beginning in childhood.

See also AMBLYOPIA; MELANOCYTE.

alopecia The clinical term for HAIR loss. There are numerous forms and causes of alopecia, which may be localized or widespread, temporary or permanent. Though alopecia is emotionally traumatic for many people, it does not affect health in any way though may reflect underlying health condi-

tions. Common forms of alopecia include the following:

- Androgenic alopecia, or male pattern hair loss, in which a man's hairline recedes from the temples and forehead and thins on the crown in a characteristic pattern that may culminate with a fringe of hair remaining along the sides and back of the head. Hair loss is permanent. Androgenic alopecia is hereditary and commonly begins in midlife, though may begin as early as a man's mid-20s. Researchers believe androgenic alopecia results from a combination of genetic predisposition and naturally declining TESTOSTERONE levels.
- Female pattern alopecia, in which a woman's hair gradually thins on the top and sometimes back of her head. Hair loss is permanent. Researchers believe female pattern alopecia results from hormonal changes (loss of ESTROGENS and testosterone) that occur following MENOPAUSE.
- ALOPECIA AREATA, an autoimmune disorder in which the body's IMMUNE RESPONSE attacks clusters of hair follicles, temporarily impairing their ability to produce new cells. Alopecia areata may affect any part of the body and occasionally the entire body. Hair loss is temporary, though may be long term.
- Toxic alopecia, which results from exposure to substances that impair the ability of the hair follicles to generate new cells. The most common sources of such exposure are radiation therapy and chemotherapy treatments for cancer. Other causes include vitamin A toxicity and medication side effects, such as from retinoid preparations to treat acne. The extent of hair loss depends on the toxic agent, ranging from localized (such as with radiation therapy to the head) to nearly complete (such as with chemotherapy). Hair growth returns when the toxic exposure ceases.

Scarring, such as occurs as a result of BURNS, wounds, and certain AUTOIMMUNE DISORDERS, destroys the hair follicles so hair loss in such areas is permanent. Conditions and circumstances that damage but do not destroy the follicles often allow hair growth to resume. Medical treatments that stimulate follicle activity can accelerate the return of hair in many such situations.

CONDITIONS ASSOCIATED WITH ALOPECIA

radiation exposure	CHEMOTHERAPY
TRICHOTILLOMANIA	tinea capitis
PREGNANCY	MENOPAUSE
HYPOTHYROIDISM	high FEVER
INFECTION or serious illness	scars from wounds or BURNS
excessive hair care and styling	SUNBURN and sun exposure
AUTOIMMUNE DISORDERS	DISCOID LUPUS ERYTHEMATOSUS (DLE)
hormonal changes	MALNUTRITION
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	hair coloring and styling products
stress	
FOLLICULITIS	

Symptoms and Diagnostic Path

Hair loss is the primary symptom of alopecia. The pattern and rate of hair loss help determine the nature of the underlying cause. When alopecia is male pattern or female pattern hair loss, the doctor can make the diagnosis on the basis of appearance. When the cause of hair loss is uncertain, the doctor may biopsy several sites on the scalp, both with and without hair, for microscopic examination. A comprehensive health history and medical examination are important to identify any potential systemic or general health causes for hair loss. Preliminary findings determine what, if any, further testing is necessary.

Treatment Options and Outlook

Treatment first targets any underlying condition that may be responsible for hair loss. In many situations of alopecia related to other health conditions, hair growth will resume without medical intervention. People who are sensitive about their appearance during the period of temporary alopecia may choose to wear hairpieces, hair weaves, wigs, scarves, or hats until their hair returns. Topical products to stimulate hair growth, such as minoxidil (Rogaine) and finasteride (Propecia), sometimes hasten the return of hair follicle function. Such products are often the first choice of treatment for male or female pattern hair loss as well as many forms of nonscarring alopecia. However, hair growth typically continues only for as long as treatment continues.

Minoxidil and finasteride can cause serious BIRTH DEFECTS when they enter the system of a woman who is pregnant. Women of childbearing age generally should not use or handle these products.

Hair replacement methods surgically relocate scalp SKIN with abundant, productive hair follicles to areas of the scalp where there is hair loss. Though these methods cannot restore hair growth to its previous patterns and thickness, they can provide satisfactory results for many people. The color and consistency of the hair influences the success of hair replacement. As well, the scalp must contain adequate areas of productive hair follicles to serve as donor sites.

Risk Factors and Preventive Measures

Risk factors for alopecia include AUTOIMMUNE DISORDERS, toxic exposures, stress, heredity, and aging. Efforts to maintain healthy skin help support productive hair growth though cannot prevent most forms of alopecia. Treating any underlying condition that causes alopecia often results in the return of hair.

See also FOLICULITIS; HIRSUTISM; LICHEN PLANUS; SCAR; STRESS AND STRESS MANAGEMENT; TINEA INFECTIONS.

alopecia areata A form of HAIR loss (ALOPECIA) that results from an autoimmune disorder in which the IMMUNE SYSTEM attacks clusters of hair follicles, halting hair growth. The clusters typically appear as circular patches of hairless SKIN, which are most noticeable when they occur on the scalp though can occur anywhere on the body. Hair growth within the affected follicles may remain interrupted for months to years; the timing and pattern of attacks seem to be random. Hair growth will eventually resume without treatment, though sometimes years after symptoms first begin. The extent of hair loss varies widely among individuals, ranging from a few isolated patches to the entire scalp or total body. Some people also experience small pits, called stippling, in their fingernails and toenails. Alopecia areata can affect people of any age and is more common in people who have other AUTOIMMUNE DISORDERS.

Researchers suspect an interaction between genetic and environmental factors is responsible for alopecia areata, though they do not yet understand the precise mechanisms. Alopecia areata does not affect health in any way other than hair growth; however, the cosmetic result (particularly scalp involvement) often distresses people who have the condition. Treatments to stimulate follicle activity sometimes can restore normal hair patterns when hair loss is mild to moderate. Cosmetic solutions such as wigs or hairpieces may produce more satisfactory results than medical interventions when the affected areas are extensive.

THERAPIES FOR ALOPECIA AREATA

site-specific cortisone injections	oral CORTICOSTEROID MEDICATIONS
topical minoxidil	topical anthralin
topical IMMUNOTHERAPY	
wigs and hairpieces	

See also PSORIASIS.

angioma A noncancerous tumor formed of BLOOD vessels (hemangioma) or LYMPH VESSELS (lymphangioma). Angiomas visible on the SKIN are common and may appear as circular, red growths (cherry angiomas) or weblike networks of blood vessels just beneath the surface of the skin (spider angiomas). Angiomas generally remain small and seldom present health complications. Because it contains such a rich blood supply an angioma may bleed profusely when cut or in a location that receives frequent irritation such as from clothing that rubs or constricts it. The dermatologist may remove an angioma that often bleeds or that the person finds cosmetically unacceptable. Common methods of removal include electrical desiccation (applying a slight electrical current to the angioma) and liquid nitrogen (which freezes the angioma). Angiomas occur more frequently in older adults (beyond age 50), though can develop at any age.

See also ARTERIOVENOUS MALFORMATION (AVM); TELANGIECTASIS; VARICOSE VEINS.

athlete's foot See TINEA INFECTIONS.

B

baldness See ALOPECIA.

bedsore See DECUBITUS ULCER.

birthmark A discoloration on a newborn's SKIN present at, or that emerges within a few weeks of, birth. Birthmarks are either vascular (composed of BLOOD vessels and red in color) or pigment (patches of skin that differ in color from the surrounding skin). Though some birthmarks, especially large ones, may be permanent, many fade to become faint or unnoticeable by about age 10 years. Most birthmarks do not present any health problems, though large or obvious birthmarks often arouse concern for cosmetic reasons. Occasionally vascular birthmarks arise in sites where they can interfere with vision (when near the EYE or on the eyelid), BREATHING (when near the entrance to the NOSE), or feeding (when on the lips).

Symptoms and Diagnostic Path

Most birthmarks are present at, or appear shortly following, birth. Some vascular birthmarks may not appear for several months after birth. When this is the case, the birthmark appears suddenly and grows rapidly, then remains at a steady size. Many vascular birthmarks then disappear as the child grows older. The doctor can identify most birthmarks based on physical appearance. The doctor may choose to conduct MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN when there is a cavernous hemangioma because this kind of blood vessel tumor (noncancerous) can occur within internal organs such as the LIVER or BRAIN and creates a risk for HEMORRHAGE (uncontrolled bleeding), or the doctor may perform a biopsy (take a tissue sample to examine under a microscope) of lesions of questionable composition. Multiple café au lait spots (six or more) can suggest NEUROFIBROMATOSIS, a genetic disorder, and require further evaluation. Congenital dermal melanocytosis (Mongolian spot) often has the appearance of a large bruise (ECCHYMOSIS), sometimes raising concerns about CHILD ABUSE among those who are not familiar with this birthmark. A health-care provider can quickly distinguish the mark and determine that it is not a bruise.

Any change in the size, color, or characteristics of a birthmark, especially a NEVUS (mole), requires prompt medical evaluation to check for malignant melanoma or other SKIN CANCER.

Treatment Options and Outlook

Most birthmarks fade by ADOLESCENCE, making treatment unnecessary. The doctor may choose to surgically remove nevi (moles) that are large or in locations where they are subject to irritation from clothing or movement, to prevent them from evolving to SKIN CANCER. Port wine stains (flat hemangiomas) are often emotionally distressing when they occur on the face. The dermatologist may use laser therapy to shrink and seal off the blood vessels causing the port wine stain, diminishing its prominence. Cover-up cosmetics are also an option. Children are particularly sensitive about having obvious birthmarks and may need emotional support. Birthmarks are very common, with some experts estimating that about a third of infants are born with them.

Risk Factors and Preventive Measures

Birthmarks appear to be random and common, with as many as a third of newborns having at least one. Because researchers do not know what

BIRTHMARKS

Clinical Name	Type	Common Names	Characteristics
capillary hemangioma	vascular	strawberry hemangioma	red discolorations that resemble strawberries most common on the face, back, chest, and back of the neck may be nonexistent at birth, then within a few weeks appear and rapidly grow generally fade by age 9
cavernous hemangioma	vascular	none	purple or reddish blue cluster of blood vessels beneath, rather than on the surface of, the SKIN may be quite large, with a spongy consistency may exist within internal organs such as the LIVER, BRAIN, and BONE present at birth or appears within a few days of birth susceptible to possibly profuse bleeding with trauma may require surgical removal
congenital dermal melanocytosis	pigment	Mongolian spot, Mongolian blue spot	common among infants with dark skin dusky blue coloration, can cover a large area most often appears on the lower back or buttocks present at birth or appears within a few days of birth generally fades by age 12
congenital NEVUS; giant congenital nevus	pigment	mole	cluster of pigmented cells may be flat or raised may have HAIR growing from it (called hairy nevus) increased risk for malignant melanoma when > 20 centimeters (giant congenital nevus)
nevus flammeus	vascular	stork bite, salmon patch	small, pink, irregular discolorations of the skin most common on the face and back of the neck may be nonexistent at birth, then within a few weeks appear and rapidly grow generally fade by age 4
nevus flammeus	vascular	port wine stain	most often appears on the face persists into adulthood
hyperpigmented MACULE	pigment	café au lait spot	coloration similar to coffee with milk faint appearance at birth, becomes more prominent by age 3 More than five or six spots may suggest neurofibromatosis

causes them to occur, there are no known measures for preventing them. Any changes in a birthmark that has been stable in size and appearance warrant a doctor's evaluation to determine whether the changes signal skin CANCER. Early detection and treatment are especially crucial for malignant melanoma, in which a NEVUS becomes cancerous, as this cancer can be aggressive and lethal when untreated. Birthmarks themselves do not present any risk to overall health.

See also ANGIOMA; GENETIC DISORDERS; LESION.

blister A fluid-filled pocket that develops between the layers of SKIN in response to friction or pressure. Blisters are most common on the feet and hands though can develop nearly anywhere on the body. Blisters often hurt. Their outer layer of skin is vulnerable to tearing, which allows the fluid to leak out. Though the blister may then feel better because there is less pressure, the break in the skin's surface gives BACTERIA access to the inner layers of tissue and establishes a risk of INFECTION.

An intact blister usually will heal within three to five days as the body reabsorbs the fluid and repairs the damaged skin. A ruptured blister is an open wound that requires appropriate WOUND CARE, such as cleansing with mild soap and water and possibly antibiotic ointment and a bandage. The most effective treatment for blisters is prevention such as wearing gloves or thick socks and properly fitting shoes or boots. An area of the skin that repeatedly forms a blister often develops a CALLUS, an accumulations of keratocytes, which increases the skin's thickness and improves its ability to withstand friction or pressure.

See also BULLA; CORNS; DECUBITUS ULCER; KERATOCYTE.

botulinum therapy Injections of botulinum neurotoxin to selectively paralyze MUSCLE fibers. The bacterial strain *Clostridium botulinum* produces several forms of paralytic toxin, some of which can cause serious or fatal poisoning (BOTULISM) when ingested. The toxin works by blocking the release of acetylcholine, a NEUROTRANSMITTER that facilitates NERVE signals between muscle cells and the BRAIN. The blockade prevents the muscle cells from contracting. Botulinum therapy products currently available in the United States contain a weakened and purified solution of botulinum neurotoxin A (Botox) or botulinum neurotoxin B (Myobloc).

Botulinum therapy became therapeutically acceptable in the United States in 1990 when the US National Institutes of Health (NIH) issued a consensus statement outlining the clinical applications for its use (*Clinical Use of Botulinum Toxin* [NIH Consensus Statement]. 1990. November 12–14; 8[8]:1–20). These uses include treatment for neuromuscular disorders such as DYSTONIA, BLEPHAROSPASM, CEREBRAL PALSY, STRABISMUS, TORTICOLLIS, MULTIPLE SCLEROSIS, and PARKINSON'S DISEASE, as well as spasms that result from TRAUMATIC BRAIN INJURY (TBI) OR SPINAL CORD INJURY.

An outgrowth of these applications was the discovery that botulinum therapy causes SKIN WRINKLES to lessen or disappear. In 2002 the US Food and Drug Administration (FDA) approved botulinum therapy as a cosmetic treatment for forehead wrinkles (frown lines). Cosmetic applications are becoming increasingly common, with many dermatologists using botulinum therapy to reduce wrinkles around the eyes and other areas of the face and body. In 2004 the FDA approved botulinum therapy for HYPERHIDROSIS, a disorder of the SWEAT GLANDS that results in profuse sweating. The effects of botulinum therapy last about four to six months. Risks are slight and may include localized INFECTION and temporary weakness of the injected muscles.

See also BACTERIA; BLEPHAROPLASTY; CHEMICAL PEEL; RHYTIDOPLASTY.

bruise See ECCHYMOSIS.

bulla A large (5 millimeters or greater) blister-like formation, raised and fluid filled, that may hurt or itch. INFECTION, contact irritants, IMMUNE RESPONSE, and systemic health conditions may cause bullae. Bullous DERMATITIS may result from contact with plants such as poison ivy, oak, or sumac. To determine the cause of bullous eruptions, the doctor may biopsy a bulla (remove a small section for examination under the microscope) or perform tests to look for immune proteins. Tense bullae form in the deeper layers and are less likely to rupture. Flaccid or loose bullae form in the superficial layers of the skin and are fragile, making them more likely to tear.

Treatment generally is twofold, targeting the underlying cause as well as aiming to relieve symptoms such as itching and the bullous swellings. Topical CORTICOSTEROID MEDICATIONS often help the symptoms and sometimes the underlying cause when it is an immune response or autoimmune disorder. ANTIBIOTIC MEDICATIONS, often both topical and oral, are necessary to treat bullae that arise from bacterial infection or that become infected. Healed bullae may leave indentations or scars, especially if they were infected.

HEALTH CONDITIONS ASSOCIATED WITH SKIN BULLAE

adverse DRUG reaction	BULLOUS PEMPHIGOID
contact dermatitis	DERMATITIS herpetiformis
DIABETES	EMPHYSEMA
hereditary AUTOIMMUNE DISORDERS	IMPETIGO
PEMPHIGUS	STAPHYLOCOCCAL SCALDED SKIN SYNDROME
TOXIC EPIDERMAL NECROLYSIS	warfarin reaction

See also BLISTER; CALLUS; CELLULITIS; ICHTHYOSIS; PAPULE; URTICARIA; VESICLE.

bullous pemphigoid An autoimmune disorder in which itchy bullae (blisterlike formations) develop on the SKIN. Bullous pemphigoid is more common in people age 50 and older, and typically occurs in those who are 70 or older. The bullae tend to concentrate in areas where there are skin folds, such as the groin and the creases of the elbows and knees. The skin around the bullae may be red and tender. The condition is self-limiting, which means it will improve on its own. However, the bullae are very uncomfortable; medical intervention targets relieving their discomfort and hastening the condition's regression and resolution. The doctor will likely biopsy several of the bullae to obtain a definitive diagnosis. Treatment with topical and oral CORTICOSTEROID MEDICATIONS reduces the IMMUNE RESPONSE and improves symptoms. The B vitamin niacinamide also provides additional relief for some people. The bullae usually heal without scarring. In most people the bullae heal within a few months, though occasionally the course of disease may run several years.

See also AUTOIMMUNE DISORDERS; BULLA; PEMPHIGUS.

C

callus An accumulation of keratocytes that form a thickened area of SKIN in response to repeated friction or pressure, typically at the site of repeated blistering. A callus may be a different color than the surrounding skin, often grayish or yellowish. Calluses are most likely to develop on the palms, fingers, fingertips, heels, and balls of the feet. Most calluses are not painful and help protect the skin from blisters and other friction-related injuries. Calluses do not require medical intervention unless they cause PAIN. Applying aloe or a moisturizing skin lotion and gently rubbing the callus with a pumice stone while in the shower or bath are measures that can contain the size and thickness of calluses. Wearing gloves to protect the hands and well-fitting socks to protect the feet can help prevent a BLISTER and resulting callus from forming.

See also CORNS; KERATOCYTE.

carbuncle Clusters of infected HAIR follicles (furuncles) that often form an ABSCESS. Carbuncles are most common on the back of the neck and shoulders, though may form at other locations where furuncles tend to occur. Carbuncles are painful and often result in FEVER and general malaise (not feeling well). The INFECTION is deep within the layers of SKIN and generally requires treatment with an oral ANTIBIOTIC MEDICATION. The doctor may choose to lance (open with a sterile incision) the carbuncle to allow the collected pus to drain. Applying warm, moist compresses four to six times a day helps open the follicles and allow continued drainage as HEALING takes place.

Though poor PERSONAL HYGIENE can contribute to the development of furuncles and carbuncles, the primary cause of these painful sores is BACTERIA, typically *Staphylococcus*, that normally resides on the skin. Carbuncles tend to recur. People who have DIABETES are more likely to develop carbuncles because the diabetes damages the delicate blood vessels responsible for peripheral circulation, preventing the bloodstream from carrying bacteria-fighting blood cells to the site of the infection. People who have impaired immune function are also at increased risk. Untreated carbuncles can result in scars after healing or can progress to systemic infection (SEPTICEMIA).

See also CELLULITIS; FURUNCLE; SCAR.

cellulitis INFLAMMATION of the inner layers of the SKIN and the underlying connective tissues, usually the result of a bacterial INFECTION. People who have PERIPHERAL VASCULAR DISEASE (PVD), DIABETES, or other health conditions that impair BLOOD circulation have increased risk for cellulitis. Cellulitis develops when a break in the skin, such as a cut or an insect bite or sting, allows BACTERIA normally present on the surface of the skin to enter and establish infection. The offending breach often comes from something so small as to appear insignificant until infection sets in. *Staphylococcus* is the most common type of bacteria responsible for cellulitis; *Streptococcus* is sometimes responsible. Bacteria also may enter via contamination of a penetrating object such as a splinter. Cellulitis requires prompt treatment with ANTIBIOTIC MEDICATIONS to minimize tissue damage and prevent the spread of infection.

Symptoms and Diagnostic Path

Swelling, redness, and PAIN or itching are the key symptoms of cellulitis. The edges of the infection are diffuse, often making it difficult to establish a border between healthy and infected tissue. The doctor diagnoses cellulitis primarily on its appear-

ance and symptoms. Usually no blood or other laboratory tests are necessary, unless the doctor suspects systemic infection (SEPTICEMIA) or questions the causative strain of bacteria.

Treatment Options and Outlook

For moderate, localized cellulitis the typical treatment is a course of oral antibiotics with close follow-up to make sure the selected antibiotic is effective against the infection and the cellulitis is improving. Warm, moist compresses over the infected area help draw blood the area, improving the body's ability to fight the infection. When cellulitis affects a large area or multiple areas or worsens after antibiotic therapy begins, the doctor may place the person in the hospital for intravenous (IV) antibiotic therapy and continuous observation. Cellulitis in a person who is IMMUNOCOMPROMISED or otherwise debilitated requires especially aggressive treatment. Untreated or undertreated cellulitis can have serious consequences such as septicemia or GANGRENE (death of the tissue). Cellulitis also presents particular risk to people who have impaired circulation for any reason. With timely and appropriate treatment, most people recover fully.

Risk Factors and Preventive Measures

Wounds that break the skin breach the body's first line of defense against infection. Prompt cleansing of the entry site with antibacterial soap and warm water, followed with topical antibiotic ointment and a bandage, helps reduce the amount of bacteria that enter the skin and limit their ability to cause infection. Early signs of infection, such as swelling, redness, or drainage, require prompt medical intervention that may include oral antibiotic medications. People who have diabetes, PVD, and other conditions that restrict peripheral circulation should develop the practice of regularly examining the feet, lower legs, fingers, hands, and lower arms for minor wounds that could become problematic as a measure for early identification and intervention to prevent cellulitis.

See also DECUBITUS ULCER; INSECT BITES AND STINGS; NECROTIZING FASCIITIS.

chemical peel A cosmetic procedure to smooth and tighten the surface of the SKIN, typically on the face, to improve the appearance of WRINKLES, scars, ACNE, widespread ACTINIC KERATOSIS, LENTIGINES (brown spots or liver spots), dyschromia (pigmentary irregularities), and other blemishes. The dermatologist applies a chemical solution, either an acid or phenol, to the selected areas of skin. The solution BURNS the skin, causing one layer or more of skin to slough off as HEALING takes place. The new skin that replaces the old skin is smoother, tighter, and lighter in color.

Light Peel: AHA Solutions

The lightest chemical peel is an alphahydroxyl acid (AHA) solution such as lactic acid or glycolic acid. It removes the top layer of skin (epidermis) and is appropriate for treating minor skin irregularities. The dermatologist puts the mild acid on selected skin sites in a series of applications or may mix the solution into a cream or wash for weekly home use until the peel produces the desired results. An AHA chemical peel causes mild irritation and discomfort that resolves as the skin heals. It generally takes six to eight weeks to see results with an AHA peel. An AHA peel requires frequent retreatment to maintain the effect.

Moderate Peel: TCA Solution

A moderate chemical peel uses a stronger acid solution, trichloroacetic acid (TCA), to remove the top and underlying layers of skin (epidermis and upper dermis). The dermatologist applies the TCA solution in one to three sessions spread over several months. A TCA chemical peel is appropriate for treating fine facial wrinkles and pigmentary irregularities. The treated area first forms a frothy coating and then scabs or crusts. The treated area also becomes swollen and may be uncomfortable enough to require mild PAIN relief medication for several days. Full healing takes about two weeks. The effects of a TCA peel generally last a year or longer, though many people need more than one treatment to achieve the desired results.

Deep Peel: Phenol Solution

A deep chemical peel extends through the dermis, the middle layer of the skin, to the hypodermis (innermost layer of the skin). It produces somewhat of a burn effect that causes complete loss and replacement of the skin. The dermatologist

uses a phenol solution to achieve this result, which is appropriate for treating moderate facial blemishes, acne scars, sun damage, actinic keratosis, and most wrinkles. The application procedure takes about an hour, before which the dermatologist generally administers a sedating medication. Following the phenol application the dermatologist coats the treated area with petroleum jelly or other protective covering to reduce discomfort. The treated area is immediately raw and exposed, with scab formation in about 48 hours.

Swelling and discomfort are significant for a week or two after a phenol peel, and most people cannot participate in any regular activities during this time and may require assistance if the swelling causes their eyes to close. Proper care during healing is essential, and typically requires a regimen of ANTIBIOTIC MEDICATIONS and ointments to help keep the healing tissue moist and supple. The treated skin remains red and shiny for up to three months. Full healing takes four to six months, though most people can return to most normal activities in about three weeks.

The effects of a phenol peel typically last several years. The skin commonly loses its ability to produce melanin, however, making sunscreen and protective clothing such as a broad-brimmed hat essential to prevent sun damage and SUNBURN when outdoors. Most dermatologists recommend applying sunscreen daily, after healing, as a routine preventive measure. The loss of melanin also results in a permanently lighter pigmentation of the treated area. Because of this, people who have dark skin should not undergo phenol peels.

Risks and Complications

Though chemical peels can produce smoother, more youthful looking skin, they do so by first damaging the skin so it must repair itself. The risks of chemical peels include infection, scarring, and irregularities in pigmentation after healing. Some people have adverse reactions to the chemical solutions. People who are prone to cold sores or FEVER blisters are likely to develop them during the healing phase; many dermatologists prescribe ANTIVIRAL MEDICATIONS to prevent these viral outbreaks from occurring. Phenol may exacerbate ARRHYTHMIA (irregularity of the heartbeat) in people who have arrhythmia disorders.

See also AGING, INTEGUMENTARY CHANGES THAT OCCUR WITH; BLEPHAROPLASTY; BOTULINUM THERAPY; COLD SORE; DERMABRASION; LASER SKIN RESURFACING; PLASTIC SURGERY; RHINOPLASTY; RHYTIDOPLASTY; SCAR; VITILIGO.

chloasma A pattern of hyperpigmentation, often temporary, that typically affects the face. Chloasma, also called melasma, develops with elevated blood levels of ESTROGENS, such as occurs during PREGNANCY, with some oral contraceptive (birth control pill) formulations, and in chronic LIVER disease. When the cause is hormonal, the hyperpigmentation fades when HORMONE levels return to normal. Chloasma may also develop in men or women who have liver conditions such as CIRRHOSIS or HEPATITIS. The melanocytes (melanin-producing cells) in the affected areas of skin overproduce melanin, the pigment that gives SKIN its color. The hyperpigmented areas have clearly defined borders and often appear in symmetry, resulting in a masklike appearance.

The doctor diagnoses chloasma on the basis of its appearance and correlation with factors such as pregnancy or liver disease. Topical solutions such as hydroquinone and tretinoin (Retin-A) help fade the chloasma in some people, though pregnant women should not use these treatments. Both medications have potentially serious side effects and are for short-term use only (eight weeks or less). As sun exposure intensifies melanin production, dermatologists recommend wearing sunscreen (sun protection factor [SPF] 30 or greater) and shading exposed areas of skin from the sun as much as possible. Chloasma is primarily cosmetic and does not present a threat to health other than that of any underlying condition. Most chloasma resolves on its own when the underlying cause health condition changes.

See also MELANOCYTE; ROSACEA; SUN PROTECTION.

corns Growths of thickened SKIN on the tops and sides of the toes. Corns result from accumulations of keratocytes that develop in response to repeated pressure, typically from shoes that are too tight, and are the body's effort to protect the skin and underlying tissues. A corn has a hard inner core with a surrounding ring of thickened though soft skin. Corns often hurt because they

compress and irritate the nerves in the underlying tissues, and continue to grow as long as the pressure against the toes continues.

The most effective treatment for corns is prevention by wearing low-heeled shoes that fit properly. A shoe with a heel more than half an inch higher than the rest of the shoe's sole causes the foot to slide forward in the shoe, squeezing the toes and subjecting them to pressure from the sides and top. Once a corn develops, treatment focuses on softening the skin and relieving pressure against the area. Self-care measures include

- wearing flat-soled, wide-toe-box shoes
- using corn pads, donut-shaped felt or foam rings, to relieve pressure against the sensitive inner core of the corn while wearing shoes
- gently rubbing the corn with a pumice stone while in the bath or shower
- applying aloe vera gel or moisturizing lotion to the area

Large corns or corns that fail to respond to self-care measures require evaluation and possible treatment from a podiatrist (foot care specialist), who may anesthetize the corn and use a scalpel to shave away some of the overgrown skin.

See also BLISTER; CALLUS; KERATOCYTE.

cradle cap A form of DERMATITIS, also called infantile seborrheic dermatitis, in which the sebaceous structures of the SKIN oversecrete oils. The excessive sebaceous secretions trap loose, dead skin cells, forming crusts or scales. Cradle cap, as the name implies, affects young infants. Doctors believe the condition results from the surge of maternal hormones that infuse the infant's bloodstream shortly before birth, stimulating the sebaceous glands. Because the primary location of body hair on the infant is on the head, the crusts are most common on the scalp. They also may form around the eyebrows. Gentle shampooing helps keep the scalp clean. The caregiver can rub baby oil into crusted areas to soften crusts before shampooing to help remove them. Cradle cap generally clears up within a few months and does not occur after about age 12 months.

See also DANDRUFF; HORMONE; SEBACEOUS GLAND.

D

dandruff A common symptom in which the sebaceous glands on the scalp increase their activity, accelerating the SKIN's normal, continuous process of replacing itself. Consequently the skin on the scalp sheds cells at an accelerated rate, causing visible patches of collected cells that accumulate on the scalp's surface (most commonly on the top of the head) or flaking that may appear in the HAIR and on the clothing. BACTERIA and yeast (FUNGUS) normally present on the skin can irritate and inflame the sebaceous structures of the scalp, a condition doctors call seborrheic DERMATITIS. Dermatologists often diagnose seborrheic dermatitis as the underlying cause of dandruff. PSORIASIS and tinea capitis are also common causes.

Flaky, patchy SKIN on the eyebrows, around the eyelashes, and other sites on the body beyond the scalp may signal a dermatologic condition other than dandruff and requires a doctor's evaluation.

Though numerous factors may contribute to dandruff, dermatologists believe a convergence of genetics, age, hormones, and environmental conditions accounts for most cases, as these are the factors that generally influence sebaceous activity. Dandruff flare-ups are common during PUBERTY, PREGNANCY, and MENOPAUSE, periods of life characterized by hormonal surges. Dandruff also becomes more common during times of physical or emotional stress, and when external environmental conditions are cold and dry such as is typical in the winter.

Symptoms and Diagnostic Path

Light-colored patches on the scalp that flake when scratched or flakes in the hair and on the clothing are the key symptoms of dandruff. The scalp sometimes itches. The diagnostic path includes examination of the skin over all of the body to distinguish simple dry skin, which can cause flaking, from dandruff, as well as to rule out other dermatologic conditions. The dermatologist may conduct further testing, such as skin scraping or biopsy, when there is reason to suspect a condition other than one that commonly causes dandruff.

Treatment Options and Outlook

Mild dandruff—light, barely noticeable flaking that remains along the scalp or in the hair—often clears with daily shampooing and thorough rinsing. Moderate dandruff—obvious flakes in the hair and on the shoulders—may require shampooing with products that contain ingredients to curtail the growth of keratinocytes, the cells that make up most of the skin's outer layer (epidermis). Such shampoos typically contain selenium sulfide, zinc pyrithione, or coal-tar extracts. Which products are more effective seems a matter of personal preference.

Severe dandruff—flakes are always present in the hair and on the clothing—may require prescription shampoos or lotions that often contain stronger concentrations of the active ingredients that over-the-counter products contain. For very severe dandruff with INFLAMMATION of the skin and sebaceous structures, the doctor may prescribe corticosteroid drops or lotion in combination with other remedies. Stubborn dandruff may require a regimen of products to bring it under control, though most people can then keep dandruff in check with a few core products.

Recent research suggests that many people who have seborrheic dermatitis, the most common cause of persistent dandruff, may have a skin

environment that encourages a normally present fungus, *Malassezia* (also called *Pityrosporum*), to flourish in abundance. *Malassezia* subsists on sebum, an oil substance the sebaceous glands secrete. An overgrowth of *Malassezia* depletes the sebum supply, causing the sebaceous glands to increase sebum production. This in turn accelerates cell growth, generating dandruff. Shampoos and lotions containing an antifungal medication such as ketoconazole reduces the scalp's *Malassezia* population, returning cell turnover to normal.

PRODUCTS TO CONTROL DANDRUFF

coal-tar extracts	glycolic acid
ketoconazole and other antifungal shampoos	salicylic acid
selenium sulfide	tea tree oil
zinc pyrithione	topical corticosteroids

Risk Factors and Preventive Measures

Frequent or heavy use of hair products such as hairsprays and styling gels can further clog the sebaceous structures. Stress, hormones, and the environment can precipitate or exacerbate dandruff. Dandruff, or the skin conditions that establish dandruff such as seborrheic dermatitis, are more common in people who have PARKINSON'S DISEASE, though the reason for this remains unknown. People who are prone to dandruff that worsens seasonally often can minimize the severity of their symptoms by beginning therapeutic efforts before flaking becomes a problem.

See also CORTICOSTEROID MEDICATIONS; CRADLE CAP; HORMONE; KERATINOCYTE; KERATOSIS PILARIS; SEBACEOUS GLAND; STRESS AND STRESS MANAGEMENT.

decubitus ulcer An erosion in the SKIN that results from the pressure of remaining in one position for an extended period of time, commonly called a bedsore or pressure sore. The extended pressure deprives the tissue of blood circulation, allowing cells to die and the tissue to break down. Tissues over areas where the bones are near the skin are most vulnerable, such as the hips, ankles, heels, elbows, shoulders, base of the spine, and back of the head. Decubitus ulcers are a specific risk for people who have debilitating conditions or injuries that limit their mobility, particularly elderly individuals in extended-care facilities. MALNUTRITION and age-related changes to the skin result in fragility that makes the skin more susceptible to damage.

Often, measures such as frequent changes of position and soft surfaces to shelter the skin at contact points can prevent decubitus ulcers. Within contemporary quality of care standards and guidelines in health care, decubitus ulcers raise questions as to whether providers and facilities are delivering appropriate care. Undetected or untreated decubitus ulcers can result in significant tissue loss and threaten overall health. Once established, a decubitus ulcer requires aggressive medical intervention to limit permanent tissue damage and restore healthy skin.

CLINICAL STAGING OF DECUBITUS ULCERS

Clinical Stage	Presentation	Tissue Penetration
stage 1	nonblanching red area	superficial layers of skin (epidermis, first layer of dermis)
stage 2	BLISTER or open sore	full skin (epidermis and full thickness of dermis) to the underlying FASCIA
stage 3	craterlike sore that oozes or bleeds; damaged or necrotic (dead) SKIN; damage to underlying tissues	through the skin and fascia, into the supportive connective and fatty tissue
stage 4	deep ulcer that bleeds; extensive skin and tissue destruction and necrosis	through the skin, fascia, and underlying structures into adjacent MUSCLE, TENDON, and LIGAMENT, and JOINT

Symptoms and Diagnostic Path

The symptoms of decubitus ulcer depend on its stage of development. Health-care providers classify decubitus ulcers on a scale of 1 to 4, with stage 1 being the slightest level of damage and stage 4, the most significant. PAIN is not an effective measure of a decubitus ulcer's severity as the damage to the skin and underlying tissues may destroy NERVE endings. Doctors diagnose a decubitus ulcer on the basis of its appearance.

Treatment Options and Outlook

The first and most urgent action in treating decubitus ulcers is to relieve all pressure on the area. This may include using pillows, cushions, pads, and other items to support the body in positions that do not put pressure on or near the ulcer. Additional treatment may include regularly cleansing the ulcer to prevent INFECTION, or ANTIBIOTIC MEDICATIONS to treat infection that already exists. Deep ulcers (stage 3 and especially stage 4) often require surgical débridement (removing dead and damaged tissue under anesthetic).

Recovery depends on the stage of the ulcer and the general health condition of the person. With early and aggressive intervention, recovery can be complete with minimal permanent tissue damage. Stage 2 and stage 3 ulcers generally heal with some loss of tissue and scarring. Stage 4 ulcers are extensive wounds that may require multiple débridements and long-term treatment by a WOUND CARE specialist. When debilitation is long-term or permanent, the risk for recurring decubitus ulcers is high.

Risk Factors and Preventive Measures

People whose health conditions limit their ability to move parts of their bodies or confine them to wheelchairs or bed have very high risk for decubitus ulcers. Preventive measures include

- position changes every two hours when in bed and every 15 minutes when sitting in a chair or wheelchair
- air mattress with alternating compartments or air flotation mattress
- eggshell mattress or seat cushion
- sheepskin pads over bony protuberances such as the heels and elbows
- active movement at least four times a day when possible and passive range of motion exercises when active movement is not possible
- frequent (at least daily) inspection of areas vulnerable to pressure
- diligent skin hygiene, including daily cleansing and complete drying

Prompt intervention at the earliest signs of a decubitus ulcer can prevent extensive or permanent tissue damage.

See also AGING, INTEGUMENTARY CHANGES THAT OCCUR WITH; CELLULITIS; EPIDERMOLYSIS BULLOSA; GANGRENE; SCAR; SPINAL CORD INJURY; TRAUMATIC BRAIN INJURY (TBI).

dermabrasion A mechanical method for smoothing roughened or scarred SKIN. The dermabrader is a motorized burrlike device that "sands" away the layers of skin to achieve the desired result. Dermabrasion is appropriate for treating skin blemishes such as ACNE scarring or sun damage. The dermatologist administers a sedative and a local anesthetic before the procedure. After the procedure the skin is raw and tender. There is usually significant swelling and moderate discomfort that requires PAIN relief medication. The skin scabs in about 24 to 36 hours. As HEALING progresses, the scabs fall off, with the new skin pink and shiny beneath. Total healing is complete in five to six months, though most people can return to their regular activities in about three weeks. Risks and complications of dermabrasion include bleeding, INFECTION, scarring, and occasionally KELOID (overgrown SCAR) formation. Proper postprocedure care is important to encourage appropriate healing.

See also BOTULINUM THERAPY; CHEMICAL PEEL; LASER SKIN RESURFACING; PLASTIC SURGERY.

dermatitis INFLAMMATION, redness (erythema), and itching of the SKIN. Dermatitis has many causes and manifests in numerous and varied presentations, some of which may reflect conditions such as viral INFECTION, AUTOIMMUNE DISORDERS, and certain kinds of CANCER. Dermatitis may be acute (come on suddenly) or chronic (persist or recur over an extended period of time).

Atopic dermatitis A chronic condition also called eczema, atopic dermatitis typically first appears in infancy or early childhood and often persists, in periods of exacerbation and REMISSION, throughout life. Symptoms include areas of red, cracked, weepy (oozing) sorelike eruptions that eventually crust, scale, and thicken. Itching is intense. The most frequent areas of involvement are the surfaces on the inner (antecubital) surface of the elbows and the back (popliteal) surface of the knees, though atopic dermatitis can affect any part of the body. Atopic dermatitis seems to have a hereditary component, as it runs in families, and is more common in people who have hypersensitivity conditions such as ALLERGIC RHINITIS.

People who have, or who have ever had, atopic dermatitis should *not* receive vaccination against SMALLPOX that uses the vaccinia virus (the vaccine administered by health-care providers in the United States). This vaccine can cause a particularly serious eruption of atopic dermatitis.

Treatments for atopic dermatitis outbreaks include topical skin lubricants, such as ointments and lotions that help the skin retain moisture, and topical CORTICOSTEROID MEDICATIONS. The dermatologist may prescribe a course of oral corticosteroid medication (such as prednisone) for severe or resistant symptoms. Oral ANTIHISTAMINE MEDICATIONS may help control itching. Scratching excoriates the lesions, setting the stage for bacterial infection, which then requires ANTIBIOTIC MEDICATIONS.

Atopic dermatitis outbreaks vary in severity and length. Atopic dermatitis abates in some children as they reach ADOLESCENCE or early adulthood, though dermatologists believe the condition goes into an extended state of remission rather than disappears. In some adults, the only indications that atopic dermatitis persists are fissures and cracks in the skin on the palms of the hands and the soles of the feet, which may appear to be exceedingly dry skin rather than dermatitis. Coating the palms and soles with petroleum jelly at bedtime, protecting the coating with mittens and socks, often helps heal the fissures. About 10 percent of the American population has atopic dermatitis.

Contact dermatitis Numerous environmental substances, from plant resins (poison ivy) to metals (nickel, stainless steel) to bath soaps and laundry detergents, can irritate and inflame the skin. Contact dermatitis may represent an allergic response in which the IMMUNE SYSTEM, particularly the Langerhans cells located in the dermis, overreacts to a substance. Allergic contact dermatitis generally appears within 24 hours of contact, while weeks or even months of exposure to irritants may take place before causing contact dermatitis. The location of the first point of outbreak often helps narrow the field for identifying the cause.

Treatment is twofold: removing the offending irritant or ALLERGEN, and treating the symptoms. Oral antihistamine medications and topical corticosteroids typically reduce itching and inflammation. It may take up to three months for all symptoms of contact dermatitis to resolve. Contact dermatitis can be a matter of OCCUPATIONAL HEALTH AND SAFETY when the offending substance is necessary in the workplace. People who work with glues, paints, metals, plastics, latex rubber, and numerous industrial chemicals commonly develop contact dermatitis.

Exfoliative dermatitis An uncommon but serious form of dermatitis in which the epidermis (outer layer of the skin) becomes inflamed and forms scales that peel away, exfoliative dermatitis nearly always indicates systemic disease, frequently a cancer such as LEUKEMIA, cutaneous T-cell lymphoma (CTCC), or LYMPHOMA. Exfoliative dermatitis may be the earliest sign of PROSTATE CANCER, THYROID CANCER, and COLORECTAL CANCER. It also develops in people who have AIDS, and may occur as an ADVERSE REACTION to numerous medications.

Exfoliative dermatitis begins with patches of skin (lesions) that turn red and itch. Within two weeks the lesions spread to cover nearly the entire surface of the skin except the soles of the feet, palms of the hands, and face (though usually spare the mucous membranes). The scaling and dilation of blood vessels that follow significantly impairs all dermal functions from IMMUNE RESPONSE to thermal regulation (heat loss). Fluid oozes continually from the exposed dermis and the BLOOD vessels are dilated, causing excessive cooling that easily becomes HYPOTHERMIA. Damage to the pro-

tective epidermis exposes the inner layers of skin and tissues to infection.

Treatment aims to restore skin integrity and function as well as to remedy any underlying disorder. Symptomatic treatment typically includes oral antihistamines to control itching, topical corticosteroids to reduce inflammation, and warm baths. Prolonged or chronic exfoliative dermatitis may require IMMUNOSUPPRESSIVE THERAPY such as psoralen plus ultraviolet-A (PUVA) therapy or methotrexate. The success of treatment depends on identifying and treating the underlying cause. Idiopathic exfoliative dermatitis tends to recur, with periods of exacerbation alternating with periods of remission.

Nummular dermatitis Circular lesions about the size of coins that crust and weep are the distinctive hallmark of nummular dermatitis. Researchers do not know what causes the lesions to take such a precise form. Sometimes mistaken for tinea corporis (ringworm) at the onset of an outbreak, the lesions begin as red, raised circles that quickly progress. Usually the lesions remain confined to small areas, and typically recur in the same locations. Outbreaks can cause significant itching. As with other forms of dermatitis, antihistamines and topical corticosteroids help control symptoms. Severe or persistent symptoms may require a course of oral or intramuscular corticosteroids.

Seborrheic dermatitis A common cause of DANDRUFF, seborrheic dermatitis affects the sebaceous structures primarily of the head and face, notably on the scalp, behind the ears, around the eyebrows, and in the beard area on men's faces. Seborrheic dermatitis may also develop on other parts of the body that have numerous sebaceous structures, such as the chest and axilla (underarms), and typically occurs in a symmetrical pattern. Inflammation stimulates the sebaceous glands to increase sebum production, which in turn accelerates the turnover rate of dermal and epidermal cells that plug the sebaceous ducts and HAIR follicles. Key symptoms of seborrheic dermatitis include oily patches of skin that crust, scale, and flake.

Most seborrheic dermatitis is idiopathic (occurs without identifiable cause) and is more common in people between the ages of 20 and 40. Seborrheic dermatitis that occurs later in life may be a sign of PARKINSON'S DISEASE, though researchers do not fully understand this correlation. Treatments for dandruff are often effective for seborrheic dermatitis, and emphasize reducing sebum production and accumulation.

Stasis dermatitis Restricted or damaged peripheral blood circulation allows fluid to collect between the layers of the skin, causing inflammation and itching characteristic of dermatitis. The skin typically becomes discolored, turning reddish brown, and scaly as the condition persists. People who have DIABETES, VARICOSE VEINS, PERIPHERAL VASCULAR DISEASE (PVD), or INTERMITTENT CLAUDICATION have increased risk for stasis dermatitis, as do people who have restricted mobility or are bedridden. The impaired circulation limits the skin's ability to resist or fight infection, and can allow the skin to break down into ulcerations that require aggressive medical intervention. Wearing support hose, elevating the legs when sitting or lying down, and walking are measures that help reduce fluid accumulations (edema).

Symptoms and Diagnostic Path

Though each type of dermatitis has unique symptoms, all types share certain symptoms in common. These include lesions that:

- are erythematous and edematous (reddened and swollen)
- crust, weep, scale, and SCAR
- itch intensely
- recur

The dermatologist often can make the diagnosis based on the appearance, characteristics, and location of the lesions as well as the individual's age and family health history. When the diagnosis is questionable, the dermatologist may biopsy several lesions for further examination under the microscope. Tests for immune response also may be helpful for confirming a diagnosis.

Treatment Options and Outlook

Antihistamine and corticosteroid medications are the mainstay of pharmacological therapy for nearly all forms of dermatitis. Secondary bacterial infections require treatment with antibiotic medications. Most dermatitis is, or becomes, chronic. Treatment approaches strive to minimize the fre-

quency and severity of outbreaks. Though dermatitis is seldom life-threatening, it can significantly interfere with QUALITY OF LIFE. Researchers continue to explore the causes of dermatitis, looking for ways to suppress symptoms.

Risk Factors and Preventive Measures

The key risk factors for dermatitis are family history and existing allergies. Preventive measures focus on minimizing outbreaks and symptoms. Self-care approaches include

- short, warm (not hot) baths or showers
- mild, detergent-free soaps
- lubricating skin lotions, creams, and oils
- nonrestrictive clothing that allows moisture to evaporate
- restricted sun exposure
- resisting scratching

See also ICHTHYOSIS; IMPETIGO; KERATOSIS PILARIS; LESION; LICHEN PLANUS; LICHEN SIMPLEX CHRONICUS; PSORIASIS; RASH; STAPHYLOCOCCAL SCALDED SKIN SYNDROME; TINEA INFECTIONS; TOXIC EPIDERMAL NECROLYSIS; URTICARIA.

dermatofibroma A noncancerous (benign) tumor that develops in the connective tissue beneath the SKIN, most commonly on the legs and occasionally on the arms. Dermatofibromas are firm, round, and may differ in color from the surrounding skin. Most dermatofibromas cause no symptoms (other than cosmetic) and require no medical intervention unless they become tender or irritated. The dermatologist may opt to remove or scrape down a dermatofibroma in a location where it receives repeated trauma such as from shaving or rubbing against clothing. Dermatofibromas are common in adults.

See also LIPOMA.

diaper rash An irritation of the genitals and buttocks in an infant or young child who wears diapers. Diaper RASH may also affect adults who wear adult diapers or other incontinence products. Most diaper rash begins as a reaction to the chemicals in urine or feces, notably ammonia, that comes into contact with the SKIN. The skin typically appears chapped and raw. The involved area is painful and may crack and bleed. Diaper rash that lasts longer than three days often reflects an INFECTION of the skin, commonly FUNGUS (CANDIDIASIS). Untreated, persistent diaper rash may develop macerations that can result in deep ulcerations and CELLULITIS, requiring medical treatment. Mild to moderate diaper rash is very common in children who are not yet toilet trained, with nearly all children experiencing at least one episode. Diaper rash often accompanies DIARRHEA. Diaper rash occurs equally among infants who wear cloth diapers and who wear disposable diapers.

Home treatment successfully eliminates most diaper rash. Methods include

- frequent diaper changes
- cleansing the skin with gentle soap and warm water with each diaper change
- application of a moisture barrier cream or diaper rash product with each diaper change

A doctor should evaluate diaper rash that persists longer than a few days without improvement after home treatment measures.

See also DERMATITIS; FECAL INCONTINENCE; URINARY INCONTINENCE.

discoid lupus erythematosus (DLE) A chronic autoimmune disorder, also called cutaneous lupus erythematosus, in which roughly circular, reddened patches (erythematous lesions) form on the SKIN. The lesions are most common on the face, back of the neck, scalp, inner lips and mouth, and outer portions of the auditory (EAR) canals. The INFLAMMATION involves the epidermis, dermis, and HAIR follicles. When the lesions heal they leave permanent scarring, lightened pigmentation, and loss of hair (ALOPECIA) in their wake. Outbreaks may range from localized and sporadic to generalized and persistent. Cigarette smoking, heat, and exposure to sunlight precipitate or exacerbate outbreaks in many people who have DLE. About 5 percent of people who have DLE subsequently develop SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), a generalized autoimmune disorder in

which lesions can attack internal structures as well as the skin.

Symptoms and Diagnostic Path

The characteristic appearance of the skin lesions is a clear diagnostic marker for DLE. Because the same skin lesions can be an early indication of SLE, the diagnostic path includes biopsy of representative lesions as well as BLOOD tests to assess ANTIBODY status. People whose DLE lesions are primarily above the neck usually have isolated DLE. People who have DLE lesions both above and below the neck have increased risk for SLE.

Treatment Options and Outlook

The primary treatment approach for DLE is topical or injected CORTICOSTEROID MEDICATIONS. In the early stages of the condition, topical corticosteroids often limit the lesion's progression. As the condition becomes established, the lesions may not respond as well and the dermatologist may inject a corticosteroid medication directly into the lesion. Some people experience relief with medications otherwise prescribed to treat MALARIA, RHEUMATOID ARTHRITIS, and severe ACNE, as well as medications that act on the IMMUNE SYSTEM such as the corticosteroids and immunomodulators. These medications have potentially serious side effects and interact with numerous other medications. Women who are pregnant or who could become pregnant cannot take many of them, as they cause damage to the developing fetus.

The use of some of these medications is OFF LABEL USE—that is, not a use the US Food and Drug Administration (FDA) has approved though the DRUG itself has FDA approval for other uses. It is important for people who have DLE to discuss with their doctors, and to fully under-stand, the potential benefits and risks of all treatment options. Treatment approaches for DLE target symptoms though do not cure the condition itself.

MEDICATIONS TO TREAT DLE

Anti-Acne (Retinoids)	
isotretinoin	acitretin
etretinate	tazarotene
Antimalarials	
hydroxychloroquine	chloroquine
Corticosteroids	
triamcinolone	hydrocortisone
betamethasone	diflorasone
flumethasone	mometasone
desoximetasone	halcinonide
fluocinonide	amcinonide
Immunomodulators	
interferon	thalidomide
azathioprine	mycophenolate
methotrexate	dapsone

Risk Factors and Preventive Measures

Researchers do not know for certain what autoimmune mechanisms cause the lupus disorders, or what triggers them. Because DLE and SLE seem to run in families, a genetic component is likely. At present there are no known preventive measures. Though women are more likely than men to develop DLE, there are no clear risk factors for the condition other than family history. Early treatment minimizes the residual scarring, atrophy, alopecia (hair loss), and other permanent consequences the lesions can cause.

Cigarette smoking worsens the lesions, so doctors strongly advise people who have DLE and smoke to stop. Sun exposure also increases the frequency and number of lesions; liberal application of high-SPF sunscreen and sun-blocking clothing can mitigate this effect.

See also AUTOIMMUNE DISORDERS; LEUKOPLAKIA; LESION; LICHEN PLANUS; SARCOIDOSIS; SJÖGREN'S SYNDROME; SMOKING CESSATION; SUN PROTECTION.

dry skin See ICHTHYOSIS.

E

eczema See DERMATITIS.

ecchymosis The clinical term for a bruise. Ecchymosis occurs when there is bleeding into the layers of the SKIN, causing discoloration and sometimes swelling and discomfort. The injured area typically undergoes several, and sometimes vivid, color changes during the stages of HEALING. Ecchymosis usually results from trauma to the tissue, such as a blow. Ecchymosis may also occur as a symptom of bleeding disorders, LEUKEMIA, LIVER disease, and other health conditions. Ecchymosis that develops without known trauma warrants a doctor's evaluation to determine the underlying cause.

See also BLACK EYE; PETECHIAE; PURPURA.

epidermolysis bullosa The collective term for a group of inherited SKIN disorders that result in blisterlike formations (bullae) on the skin. Severity can range from mild (a few bullae) to debilitating (bullae covering large areas of the body). Dermatologists classify epidermolysis bullosa according to the layer of the skin where the bullae originate. There are three general types of epidermolysis bullosa:

- Epidermolysis bullosa simplex involves the epidermis, the skin's outermost layer, and usually results from an autosomal dominance inheritance pattern for the gene that encodes keratin production.
- Junctional epidermolysis bullosa involves the basement membrane, a thin layer of cells that separates the epidermis and the dermis, and usually results from an autosomal recessive inheritance pattern for the gene that encodes protein structures which connect the epidermis and dermis through the basement membrane.
- Dystrophic epidermolysis bullosa involves the basement membrane as well, occurring in either an autosomal dominance or a recessive inheritance pattern for the gene that encodes collagen formation.

In all types, bullae form with friction or irritation to the skin. In the junctional and dystrophic types, this includes the mucous membranes of the gastrointestinal and genitourinary tracts. Healed bullae typically leave scars. The severity of symptoms and disease vary according to the type and, with dystrophic epidermolysis bullosa, the inheritance pattern (dominant or recessive). At present there is no cure for any type of epidermolysis bullosa.

Symptoms and Diagnostic Path

The bullae of epidermolysis bullosa are uniquely characteristic and typically begin in infancy. The skin is frail and may BLISTER or tear upon touch or contact with clothing and bedding. The bullae of epidermolysis bullosa simplex generally affect only the palms of the hands and soles of the feet. The bullae of other types may affect mucous membranes throughout the body. The repeated blistering and HEALING of junctional and dystrophic types causes scarring and tissue damage that often results in deformities. People who have junctional or dystrophic epidermolysis bullosa may also have defects of the tooth enamel and the NAILS, or be missing fingernails or toenails.

The diagnostic path includes examination of the entire skin surface and mucous tissues with biopsy to determine the level of tissue separation

in representative bullae, which distinguishes the general type of epidermolysis bullosa. Molecular examination, including DNA mutation analysis identifies the precise type. CHORIONIC VILLI SAMPLING (CVS) during PREGNANCY (removing a small tissue sample from the edge of the PLACENTA) can identify whether the FETUS has the disorder.

Treatment Options and Outlook

Treatment attempts to minimize or prevent bullae formation, heal bullae that do form, and provide necessary supportive care such as PARENTERAL NUTRITION. Healing mechanisms are often impaired, and ruptured bullae and related tissue damage can leave tissues exposed. Burn therapies such as artificial skin can provide a temporary covering to improve healing. Support groups offer forums for sharing experiences and coping methods.

People who have mild forms of disease may experience few bullae or complications and be able to enjoy fully active lives. More severe forms are debilitating or fatal. It is important though difficult to prevent ruptured bullae from becoming infected. Nutritional deficiencies are common when bullae form along the gastrointestinal mucosa, which may interfere with swallowing (bullae that form in the ESOPHAGUS) or absorption (bullae that form in the SMALL INTESTINE). The risk for squamous cell SKIN CANCER is very high among people who have junctional epidermolysis bullosa, with first appearance often in late ADOLESCENCE. Dermatologists advise frequent skin self-examinations and regular skin examinations by a dermatologist who has clinical experience with epidermolysis bullosa.

Risk Factors and Preventive Measures

Epidermolysis bullosa is a genetic disorder, so the primary risk factor is a family history of the condition. In autosomal recessive INHERITANCE PATTERNS, it is possible for each parent to carry the gene defect yet show no indications of disease or to have a mild form and not realize it. GENETIC TESTING can help families detect the presence of the gene MUTATION, and GENETIC COUNSELING can help couples in making family-planning decisions. Researchers continue to explore GENE THERAPY solutions.

See also BULLA; FAMILY MEDICAL PEDIGREE; GENETIC DISORDERS; HYPERHIDROSIS; MUSCULAR DYSTROPHY; SCAR; SKIN SELF-EXAMINATION; TEETH.

erysipelas A streptococcal INFECTION of the dermis, the middle layer of the SKIN. Infection commonly follows STREP THROAT, with the BACTERIA likely carried on the hands to the skin where a scratch or other breach allows the bacteria to colonize into an infection. The infection presents characteristic symptoms that allow prompt clinical diagnosis. These symptoms include

- redness (erythema), swelling (edema), and PAIN at the site of the infection
- clearly defined and usually raised border between the infection and healthy skin
- swelling of adjacent LYMPH NODES
- FEVER, generalized discomfort, and aching in the muscles and joints

Treatment is a course of ANTIBIOTIC MEDICATIONS, preferably penicillin unless the person is allergic, and medications to relieve pain and fever. Warm compresses help bring blood to the area, improving the effectiveness of the body's IMMUNE RESPONSE to attack the infection and increasing circulation of the antibiotic.

It is important for people to take ANTIBIOTIC MEDICATIONS prescribed to treat erysipelas as the doctor directs, and to use them until all the antibiotic is gone, to completely eradicate the streptococcal BACTERIA.

Prompt medical attention is essential as erysipelas can rapidly invade deeper tissues, causing CELLULITIS and perhaps SEPTICEMIA (bodywide infection). Untreated or undertreated streptococcal infections also present the risk for INFLAMMATION of the HEART valves (RHEUMATIC HEART DISEASE). With treatment, symptoms improve within 72 hours and the erysipelas resolves completely in 10 to 14 days. People who have DIABETES, impaired peripheral circulation, and IMMUNE DISORDERS are at increased risk for erysipelas. Preventive meas-

ures include HAND WASHING after coughing or sneezing.

See also SCARLET FEVER.

erythema multiforme A HYPERSENSITIVITY REACTION, commonly to medications and sometimes to viral INFECTION, in which circular, weltlike lesions resembling targets form on the arms, hands, legs, and feet. Lesions also often form on and around the lips and inside the MOUTH. The center of the LESION is typically pale and blistered, surrounded with a reddened (erythematous) middle ring. The outer ring often has a purplish tint, giving it a bruiselike appearance. Lesions typically begin erupting within three days of the causative exposure, rising suddenly. Some people experience tingling, itching, or a burning sensation at the site of the lesion.

Common causes of erythema multiforme include

- infection with the HERPES SIMPLEX VIRUS
- ANTIBIOTIC MEDICATIONS
- ANTISEIZURE MEDICATIONS
- aspirin and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)
- numerous other medications

The uniquely characteristic lesions in provide fairly conclusive diagnosis. The causative agent may be clear, such as a recently taken medication, or remain unknown (idiopathic). Most erythema multiforme outbreaks are self-limiting and clear up two to three weeks after exposure to the causative agent ends. Treatment to provide relief from discomfort may include ANTIHISTAMINE MEDICATIONS for itching, ANALGESIC MEDICATIONS for PAIN relief, and topical corticosteroids for INFLAMMATION. Nearly always the lesions heal without scarring or other complications. Prevention of future outbreaks is difficult as there are so many potential causes.

See also TOXIC EPIDERMAL NECROLYSIS; URTICARIA.

erythema nodosum The eruption of red nodules along the top surfaces of the lower legs (shins). Erythema nodosum is nearly always a symptom of an underlying condition, often a streptococcal INFECTION, and represents INFLAMMATION of the fatty tissue at the foundation of the SKIN. Other symptoms include FEVER, PAIN and swelling in the joints, and generalized discomfort and malaise. Erythema nodosum occurs most commonly in young adults between the ages of 18 and 30.

The initial eruption of nodules may clear in six to eight weeks, though outbreaks tend to recur over months to years. Over the course of HEALING the nodules change color from their original bright red to bluish red and ultimately yellow, resembling bruises, before fading completely. The doctor diagnoses erythema nodosum primarily on the basis of its appearance, though may run BLOOD tests to look for evidence of AUTOIMMUNE DISORDERS or infection that may underlie the outbreak. Treatment targets the underlying cause and may include ANTIBIOTIC MEDICATIONS when there is infection or anti-inflammatory agents such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve swelling, pain, and fever.

See also JOINT; NODULE; TUBERCULOSIS.

erythrasma A chronic bacterial INFECTION of the epidermis (outer layer of the SKIN) that produces scaly, brownish red patches that often itch. The patches may occur anywhere on the body though are most common in skin folds and moist areas such as the underarm (axilla) and groin. When

CONDITIONS ASSOCIATED WITH ERYTHEMA NODOSUM

STREP THROAT	rheumatic FEVER	SCARLET FEVER
Hodgkin's LYMPHOMA	Hansen's disease	bacterial infection
fungal INFECTION	adverse reaction to sulfonamides	PREGNANCY
ADVERSE REACTION to sulfonylureas	oral contraceptives	HISTOPLASMOSIS
INFLAMMATORY BOWEL DISEASE (IBD)	non-Hodgkin's lymphoma	SARCOIDOSIS

viewed under ultraviolet light, the areas of infection appear a deep coral color. *Corynebacteria*, BACTERIA normally present on the skin, are responsible for the infection. People who have DIABETES or OBESITY are especially susceptible to erythrasma. Treatment is topical and sometimes oral erythromycin, an antibiotic medication, which completely eliminates the infection within 10 to 14 days. As with all antibiotics, it is important to take the erythromycin (or other prescribed antibiotic) as the doctor directs and until the medication is gone. Erythrasma may recur (come back) if the environment of the skin continues to support the growth of *Corynebacteria*.

See also ANTIBIOTIC MEDICATIONS; CELLULITIS; ERYSIPELAS.

F–G

facelift See RHYTIDOPLASTY.

Fitzpatrick skin type A commonly used classification system for identifying a person's SKIN characteristics, particularly the likelihood for SUNBURN and developing ACTINIC KERATOSIS and SKIN CANCER. Dermatologists also use Fitzpatrick skin type as a factor in determining appropriate cosmetic procedures to treat skin blemishes and WRINKLES.

See also SKIN SELF-EXAMINATION.

folliculitis An infected and inflamed HAIR follicle. Folliculitis may involve a single follicle or a number of follicles in proximity, and begins with a reddened bump at the site of the follicle that soon progresses to a PUSTULE containing a collection of fluid and cells (pus). The site often hurts or itches. Most folliculitis is idiopathic—that is, it develops without identifiable cause. However, a number of risk factors can precipitate its occurrence. Among them are

- OBESITY
- HYPERHIDROSIS
- DIABETES
- DERMATITIS and SKIN irritations
- long-term topical corticosteroid use
- ABRASIONS
- immunosuppressive disorders such as HIV/AIDS

Warm compresses applied to the site several times a day may resolve isolated folliculitis. Folliculitis that persists or involves multiple hair follicles requires treatment with topical and oral ANTIBIOTIC MEDICATIONS. Most folliculitis improves within a few days of antibiotic therapy, though it is important to take the full amount of medication

FITZPATRICK SKIN TYPE CLASSIFICATIONS

Type	Skin characteristics	Sun exposure
type I	very pale or ruddy; numerous freckles	always BURNS, never tans; severe SUNBURN (blisters) with unprotected exposure; high risk for SKIN CANCER
type II	pale or light-toned; some freckles mostly on face, shoulders, arms, hands	usually burns, lightly tans; moderate sunburn (redness) with unprotected exposure; increased risk for skin cancer
type III	olive	sometimes burns, moderately tans; mild sunburn (pinkness) with unprotected exposure; moderate risk for skin cancer
type IV	light brown	seldom burns, easily tans; low risk for skin cancer
type V	brown	rarely burns, darkly tans; seldom develops skin cancer
type VI	dark brown to brownish black	never burns; rarely develops skin cancer

as the doctor directs. In people who frequently have folliculitis or who are on long-term antibiotic therapy such as for ACNE, the INFECTION may resist the common first-line antibiotics, requiring further therapy with a different antibiotic. Folliculitis usually heals without scarring or residual complications.

HOT TUB FOLLICULITIS

The hot, moist environment of a hot tub is the ideal incubator for various BACTERIA, notably the *Pseudomonas aeruginosa*. The warm water of the hot tub opens the pores, giving the bacteria access to the HAIR follicles. When the pores close after leaving the hot tub, they trap *P. aeruginosa,* which thrives in the moist setting. Folliculitis results, often appearing on the SKIN the same pattern of the clothing worn in the tub.

See also CARBUNCLE; FURUNCLE; PSEUDOFOLLICULITIS BARBAE.

freckles See LENTIGINES.

frostbite Damage to the SKIN that results from prolonged exposure to extremely cold temperatures. Frostbite occurs when the fluid in cells crystallizes into ice, causing the skin and often the underlying tissues to freeze. The fingers, hands, toes, feet, NOSE, and ears are most vulnerable to frostbite. People who have impaired peripheral circulation are at increased risk. Frostbite also can damage blood vessels, interrupting the blood supply. When this occurs, GANGRENE (tissue death) and subsequent loss of the body part are significant threats.

Symptoms and Diagnostic Path

Any loss of feeling following extended exposure to the cold raises suspicion of frostbite and is the first factor to consider when evaluating potential frostbite. The ice crystals that form cause the skin to become hard, pallid, and cold to the touch. There is loss of feeling and function, and the skin may BLISTER. Skin that has remained frostbitten for a long time may already be gangrenous or necrotic (blackened and dead). As it warms, frostbitten

FROSTBITE SEVERITY

Degree of Damage	Characteristics	Recovery Implications
first degree	spots of whitened, hardened SKIN involving primarily the epidermis erythema (redness) of adjacent skin; localized edema (swelling) distorted or absent sense of touch or clumsy movements	recovery with no residual complications
second degree	areas of whitened, hardened skin involving the epidermis and dermis erythema of adjacent skin; regional edema loss of feeling and movement fluid-filled blisters	recovery with some residual complications (scarring)
third degree	white, hard skin with frostbite extending through the layers of the skin and into the subcutaneous tissue regional edema loss of feeling and movement blood-filled blisters	recovery with moderate residual complications (tissue loss and scarring)
fourth degree	white, hard skin with frostbite extending through the skin and into supporting tissues and structures GANGRENE or necrosis; regional edema	significant loss of tissue, with AMPUTATION likely

skin turns red and BURNS or hurts, sometimes severely.

Treatment Options and Outlook

Prompt treatment is essential to save the affected tissue and body parts. When possible, a doctor should evaluate the situation and implement warming procedures for maximum recovery. To protect body parts until the person receives medical treatment, wrap them in sterile bandages (separating the fingers and toes, if affected). When immediate medical attention is not possible, warming the frostbitten areas should only be undertaken when they cannot refreeze.

Refreezing does more damage than allowing the area to remain frozen. Do not thaw frostbite unless the area can remain warm.

To warm frostbite, place the affected parts under gently running warm water for 20 to 30 minutes. The water temperature should be 8º to 10ºF above normal body temperature or about 108ºF, which feels warm but not hot to someone whose skin temperature is normal. For frostbitten ears, cheeks, or nose, apply cloths dipped in warm water. Do not use dry heat, as it will further damage the skin and tissues. Severe frostbite is likely better left for emergency care providers to treat because tissue damage is likely to be extensive.

The thawing process can be extremely painful, and may require PAIN relief medications. Superficial frostbite (first and second degree) usually heals with few or no residual consequences. Frostbite that extends deeper than the layers of the skin (third and fourth degree) can destroy MUSCLE, connective tissue, joints, and BONE, and may necessitate AMPUTATION or surgery to clean away necrotic tissue. A full damage assessment may not be possible for six to eight weeks, as it may take that long for tissue to demonstrate whether it will recover or die.

Risk Factors and Preventive Measures

People who spend extended time outdoors in cold weather, such as for employment or recreation, risk frostbite when exposure time extends beyond what clothing can protect. Wetness increases the risk. People who are very young or very old or who have DIABETES, PERIPHERAL VASCULAR DISEASE (PVD), RAYNAUD'S SYNDROME, untreated or undertreated HYPOTHYROIDISM, OR MALNUTRITION may develop frostbite far more rapidly and severely. Preventive measures include protective clothing appropriate for the weather conditions and limiting exposure when temperatures are extremely cold.

See also HYPOTHERMIA.

furuncle An infected HAIR follicle, commonly called a boil. A furuncle develops when BACTERIA normally present on the surface of the SKIN (typically staphylococcus) causes a collection of dead cells and fluid (pus) to block the follicle. The blocked follicle becomes reddened, inflamed, enlarged, and usually quite painful. Furuncles are most likely to develop in the underarm area, groin, hairline at the back of the neck, and, in men, the beard area of the face.

Most furuncles improve with frequent applications of moist heat, which helps open the follicle and drain the collected pus. A typical furuncle heals on its own in 7 to 10 days, though a large furuncle may take longer. A furuncle that does not improve within 10 days warrants a doctor's evaluation and may require lancing (a small incision to drain the INFECTION) or ANTIBIOTIC MEDICATIONS. People who have DIABETES or who are IMMUNOCOMPROMISED are more likely to develop furuncles.

Furuncles tend to recur. Preventive measures include reducing irritation from clothing and regular cleansing with an antibacterial soap. Prompt treatment at the earliest indication of a furuncle can minimize or head off the infection's development. A large furuncle may leave a SCAR after it heals, though most furuncles heal without scarring.

See also CARBUNCLE; FOLLICULITIS; INGROWN HAIR; PSEUDOFOLLICULITIS BARBAE.

goose bumps A bumpy texture to the SKIN, also called gooseflesh, that results when the erector muscles in the HAIR follicles contract, causing the hair to "stand up." Goose bumps occur when a person becomes chilled or fearful, a vestigial response no longer physiologically useful in humans. The physiologic mechanism that causes goose bumps, called the pilomotor REFLEX or pilo-

erection, is involuntary. Researchers believe it is in part the consequence of the release of stress hormones, primarily EPINEPHRINE (also called adrenaline), which stimulates the HYPOTHALAMUS. In other mammals the pilomotor reflex raises the hair or fur for warmth by trapping air near the skin's surface or to present an intimidating appearance by making the animal appear larger than it is. Goose bumps often accompany shivering, rapid and involuntary muscle contraction to generate heat.

See also HORMONE; METABOLISM; MUSCLE; THYROID GLAND.

granuloma telangiectaticum A noncancerous vascular tumor, also called a lobular capillary hemangioma or GRANULOMA pyogenicum, made up of entangled capillaries. A granuloma telangiectaticum appears suddenly as a shiny red NODULE that bleeds easily with bumping or irritation and may itch or hurt. Doctors typically remove these growths because of their tendency to bleed and to confirm the diagnosis through biopsy (examination of a tissue sample under the microscope). The cause of granuloma telangiectaticum remains uncertain; in some people the growth arises following trauma to the site, though the nodules most often occur without a known precipitating event. The growths may recur.

See also ANGIOMA; SKIN SELF-EXAMINATION; TELANGIECTASIS.

H

hair The fibers that grow from the hair follicles. Not far above the root of the hair follicle the cells that form the hair fiber are dead, hardened into their shape through compression within the follicle as new cells emerging from the hair's root push them upward. A hair fiber is five or six cells in thickness and varies in length, depending on its location. Hair on the head can grow to several feet in length, whereas the hair of the eyelashes is generally no longer than about a quarter of an inch long. The hair does not require nourishment from the body, though the secretions of the sebaceous glands help moisturize the hair fibers to keep them supple.

Genetic encoding determines the characteristics of the hair, from how rapidly it grows to whether it is curly or straight. Hair covers all SKIN surfaces except the palms of the hands and the soles of the feet, though is most prominent on the head and, after PUBERTY, in the pubic region, on the legs, and under the arms. Men typically have darker, coarser body hair than women. Specialized hairs line the auditory canals and the inside of the NOSE, functioning to remove debris from these structures.

Like the skin, the hair provides clues to the health of the body. Numerous conditions can change the characteristics of the hair. Such changes reflect circumstances that affect the hair follicles in some way, from physical damage, such as BURNS or scars that can destroy follicles, to immune or disease processes that attack the follicles and disrupt hair growth. Physical stress such as the body experiences with major injury, illness, or surgery can cause various changes in the hair, from altered color and consistency to hair loss.

The hair's characteristics also change with aging. By midlife the hair typically starts to lose the melanocytes that give it color. Sebum (the natural oil that lubricates the hair follicle) production slows, allowing the hair to become dry. Sun exposure also can alter the hair, lightening its color or extracting moisture to make it brittle. Hair-care products can help restore moisture to the hair on the head as well as to the skin of the scalp.

HEALTH CONDITIONS THAT MAY INVOLVE THE HAIR

ADVERSE REACTION to a DRUG	ALOPECIA
ALOPECIA AREATA	ERYTHEMATOSUS (SLE)
DANDRUFF	DISCOID LUPUS ERYTHEMATOSUS
FILLICULTIS	(DLE)
FURUNCLE	HIRSUTISM
HYPOTHYROIDISM	INGROWN HAIR
KERATOSIS PILARIS	LICHEN PLANUS
MENOPAUSE	nutritional deficiencies
PREGNANCY	PUBERTY
ringworm	stress
SYSTEMIC LUPUS ERYTHEMATOSUS	toxic exposure
(SLE)	TRICHOTILLOMANIA

For further discussion of the hair within the context of integumentary structure and function please see the overview section, "The Integumentary System."

See also AGING, INTEGUMENTARY CHANGES THAT OCCUR WITH; BEZOAR; MELANOCYTE; NAILS; SEBACEOUS GLAND; SWEAT GLANDS.

hair replacement A surgical procedure, also called hair transplantation, to relocate viable HAIR follicles from sites on the scalp where they are abundant to sites where there has been permanent hair loss. The most common reason for hair replacement is androgenic ALOPECIA (male pattern hair loss). Hair replacement is nearly always a cos-

metic procedure, though may be restorative to correct damage resulting from injuries or BIRTH DEFECTS.

Surgical Procedure

Hair replacement procedures may involve tissue grafts, flaps, expansion, or combinations of these methods. The surgeon will plan the appropriate approach for each individual's situation and hair loss circumstances. The OPERATION is an AMBULATORY SURGERY, performed with local ANESTHESIA and a sedative for comfort. Most people require several operations to establish satisfactory results. Mild to moderate PAIN is common for several days following a hair replacement procedure.

Tissue grafts SKIN grafts were the original hair transplantation method. The surgeon removes a plug or slice of skin from the back or side of the head and transplants it to a hair loss site. The graft may contain from one or two to several hundred hair follicles, depending on the technique and size. With the first replacement procedure the surgeon places the grafts fairly widely apart (about one eighth inch) to allow generous BLOOD circulation. Subsequent grafts fill in the spaces. Generally, a pressure bandage holds the grafts in place for 24 to 48 hours following surgery to help the transplanted skin attach to the new site, and fine sutures (stitches) close the donor sites.

HAIR REPLACEMENT GRAFT TECHNIQUES

Type of Graft	Follicles Contained	Grafts per Session
punch graft	10 to 15	50
micrograft	1 to 2	500 to 700
minigraft	2 to 4	500 to 700
slit graft	4 to 10	500 to 700
strip graft	20 to 40	500 to 700

Tissue flaps A tissue flap relocates a substantial amount of hair-bearing skin to a single recipient site. The surgeon loosens a flap of skin near the area of hair loss, and removes a similarly sized and shaped segment of skin from the hairless scalp. The surgeon leaves one end of the flap attached and pulls the remainder of the flap over the recipient site, suturing it in place. The surgeon also sutures the edges of the donor location, which heals beneath the hair with no visible SCAR. A common variation of tissue flap hair replacement is scalp reduction, in which the surgeon removes more hairless scalp than the replacement flap covers, drawing the edges tight to pull additional hair from the sides of the head higher onto the crown of the head. Tissue flaps generally heal with less chance of rejection than grafts because they remain anchored to their original blood supply.

Tissue expansion Plastic surgeons developed TISSUE EXPANSION techniques to reconstruct major skin damage following trauma such as BURNS or major surgery, then discovered tissue expansion allows natural expansion of hair-bearing scalp for hair replacement. The surgeon loosens a segment of hair-bearing skin adjacent to an area of hairless skin to create a pouch, and inserts a special silicone balloon called a tissue expander.

Over a period of months the surgeon injects saline (sterile saltwater) into the expander, gradually increasing its size. As the expander stretches, the skin grows to accommodate it. When the area produces the desired amount of growth, the surgeon removes the expander, surgically removes a similarly sized and shaped segment of hairless scalp, and pulls the new skin over the area. Tissue expansion can relocate the greatest surface area of hair-bearing skin in a single procedure and produces the most natural-appearing frontal hairline.

Risks and Complications

Risks and complications are slight for hair replacement methods, and include excessive bleeding, INFECTION, and reaction to the anesthetic. The recipient site on the scalp also may reject the replacement tissue. Because relocation traumatizes hair follicles, they immediately enter a resting phase and shed their hair about five to six weeks following relocation. Though this is normal, many people find it alarming and worry that it signals rejection of the new hair. However, with rejection the entire segment of relocated skin fails to grow and eventually sloughs off. The surgeon can generally replace the rejected replacement tissue during the next session of surgery. When they reestablish themselves in their new sites, the follicles return to a growth phase and produce about an inch of new hair within six to eight weeks after the old hair falls out.

Outlook and Lifestyle Modifications

For the first few weeks following surgery the scalp is swollen and tender, and the replacement sites may bleed with strenuous physical activity. Surgeons recommend refraining from intense exercise or activity and contact sports for two or three weeks after the procedure. The scalp remains tender (though the swelling subsides within a few weeks) for up to three or four months, depending on the replacement method. Transplanted hair growth does not look exactly the same as the hair that previously grew from the transplant site, though most people experience satisfactory results when a qualified and experienced cosmetic surgeon performs the surgery. It generally takes a year or two from the final hair replacement procedure to see the full effects.

There must be abundant healthy hair on the back and sides of the head to serve as donor hair. Men in whom male pattern hair loss begins early in life are more likely to experience severe or total hair loss as they age. Satisfactory results from hair replacement surgery are less certain when this is the case, as the transplanted follicles may also experience hair loss. Hair loss from follicles native to the site generally continues, particularly in male pattern hair loss, which can result in irregular growth patterns and the need for further hair replacement.

See also ANALGESIC MEDICATIONS; PLASTIC SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

hidradenitis suppurativa A condition of chronic INFLAMMATION resulting from blockage of the HAIR follicles (follicular occlusion). The inflammation may involve the apocrine glands, SWEAT GLANDS that secrete fluid into the hair follicles. The hair follicles then channel the sweat to the surface of the SKIN. When sebum or cellular debris plugs the apocrine gland's opening, fluid backs up into the gland. The situation results in an INFECTION that produces a hard, painful, reddened NODULE below the skin's surface. Though the nodules will heal in three or four weeks without treatment, they often SCAR and recur. Treatment with oral ANTIBIOTIC MEDICATIONS may help control the condition though does not always clear it up. Occasionally the dermatologist needs to lance (surgically open) the nodule to allow it to drain. Dermatologists do not know what causes hidradenitis suppurativa to develop, though it is more common in people who have OBESITY.

See also ABSCESS; CELLULITIS; FOLLICULITIS.

hives See URTICARIA.

hyperhidrosis Excessive sweating that results from abnormal functioning of the nerves or BLOOD vessels that supply the eccrine SWEAT GLANDS. Hyperhidrosis characteristically involves the hands (palms), feet (soles), and axillae (underarms), though can affect eccrine sweat glands anywhere in the body. The eccrine sweat glands produce most of the body's sweat and play a key role in thermoregulation (regulating body heat). They empty their fluids (perspiration) directly to the SKIN's surface for rapid evaporation and cooling.

Stress and physical activity tend to exacerbate hyperhidrosis, particularly when it affects primarily the hands and feet. The portion of the BRAIN that regulates sweating in these areas, the cerebral cortex, is not part of the body's thermoregulation system but rather responds to emotional signals such as anxiety and fear. Hyperhidrosis may also occur as an undesired SIDE EFFECT of medications or a symptom of metabolic disorders such as HYPERTHYROIDISM and DIABETES, or health conditions such as TUBERCULOSIS and Hodgkin's LYMPHOMA. Most hyperhidrosis that arises from structural or functional anomalies of the nerves or blood vessels first appears in ADOLESCENCE, when the hormonal changes of PUBERTY stimulate sweat gland function. Hyperhidrosis that begins later in life generally arises from underlying health conditions.

Symptoms and Diagnostic Path

The primary symptom of hyperhidrosis is profusely excessive sweating. The hands and feet, when involved, may be continually wet. Sweating from the underarms and other areas of the body typically drenches clothing, requiring frequent clothing changes. The diagnostic path typically includes a comprehensive NEUROLOGIC EXAMINATION and blood tests to measure HORMONE levels. The doctor may conduct further diagnostic procedures, depending on the individual's health circumstances.

Treatment Options and Outlook

Treatment options currently available in the United States include topical products, oral medications, BOTULINUM THERAPY, iontophoresis, and, when other treatments are unsuccessful, surgery.

- Topical products block the pores of the sweat glands. Those commonly used include aluminum chloride preparations, boric or tannic acid solutions, glutaraldehyde, and potassium permanganate. These products may stain the skin and clothing. Most people apply them at night and wash them off in the morning.
- Oral medications interrupt the action of the nerves that regulate sweat gland activity. Those commonly used are anticholinergics such as propantheline and benztropine, which block the action of the NEUROTRANSMITTER acetylcholine. Dermatologists sometimes prescribe other medications such as beta-blockers and calcium channel blockers. These medications may have unacceptable side effects, however, and they are not approved for this use in the United States.
- Iontophoresis uses mild electrical current in a water-based solution to shrink the sweat gland pores and is a treatment option for hyperhidrosis of the hands and feet. Relief generally requires daily treatments over a period of several weeks.
- Botulinum therapy (localized injection of purified botulinum toxin) blocks acetylcholine, interrupting the flow of NERVE signals to the muscles that contract to push fluid from the sweat glands. The effect can last for six months or longer.
- Surgery to sever some of the nerves supplying the sweat glands, or to remove clusters of sweat glands such as in the axillae, is a treatment of last resort for severe hyperhidrosis that does not respond to other treatments. The effects are permanent.

Many people who have hyperhidrosis use combinations of these approaches to control their symptoms. Hyperhidrosis is often deeply embarrassing to those who have it, particularly adolescents. Because stress plays a key role in hyperhidrosis, stress management techniques are often helpful for coping with the condition as well as reducing the stimuli that exacerbate symptoms.

Risk Factors and Preventive Measures

When an underlying health condition is the cause of the hyperhidrosis, treating the condition eliminates the hyperhidrosis. Primary hyperhidrosis is a lifelong condition for which there are no known risk factors or preventive measures.

See also OFF-LABEL USE; STRESS AND STRESS MANAGEMENT; TINEA INFECTIONS.

I–J

ichthyosis A genetic disorder of keratinization in which the cells the SKIN sheds as part of its continual renewal cluster on the skin's surface in scale-like formations. The lesions itch and flake, and the involved surfaces of the skin become very dry, reddened, and inflamed. Ichthyosis may affect limited areas of the skin or most of the skin's surface, depending on which of several GENE mutations is responsible for the condition. Ichthyosis is chronic and lifelong, with symptoms first appearing in early childhood. Ichthyosis may be hereditary or acquired. Symptoms of hereditary ichthyosis are present at birth and can be severe, often affecting the eyes and eyelids.

The dermatologist can usually diagnose ichthyosis on the basis of its appearance, though may biopsy several lesions to confirm the diagnosis. Treatment attempts to restore moisture to the skin as well as to accelerate exfoliation (remove dead cells from the skin's surface). Lotions, creams, and ointments containing lanolin or other emollients help the skin retain moisture, which eases the itching and INFLAMMATION. Topical products that contain fruit acids such as alphahydroxy acid or lactic acid help remove dead cells.

Severe ichthyosis may require topical or oral treatment with a retinoid medication such as isotretinoin. The scaly lesions tend to overlap one another and can trap BACTERIA and other microorganisms normally present on the skin's surface, causing INFECTION that requires treatment with topical or oral ANTIBIOTIC MEDICATIONS. An ophthalmologist should provide monitoring and care to detect and promptly treat EYE symptoms to prevent permanent damage to the CORNEA and to preserve vision.

See also DERMATITIS; KERATITIS; LESION; MUTATION; PRURIGO; PSORIASIS.

impetigo A contagious bacterial INFECTION of the SKIN that most commonly affects young children. Staphylococcal or streptococcal BACTERIA are the usual culprits, typically taking advantage of breeches in the skin's integrity that result from rashes, insect bites, and other minor wounds. The infection begins as small blisters, often around the MOUTH, that itch and burn. Scratching or touching the blisters and then touching other parts of the body spreads the infection. Contact also spreads the infection to other people. After two or three days the blisters rupture, ooze, and crust. The crust is characteristically honeylike in color and appearance. The blisters remain contagious as long as they are present.

Treatment is a topical antibiotic applied to the blistered areas. The doctor may also prescribe an oral antibiotic medication when the infection extends to multiple areas of the body. The blisters begin to recede within 24 to 48 hours of initiating treatment, which eases the itching and discomfort. The blisters are no longer contagious at this stage, and generally heal completely within five to seven days. Frequent HAND WASHING with antibacterial soap and warm water helps stop the spread of impetigo among children, family members, and caregivers. Prompt cleansing and treatment of minor skin irritations reduces the opportunity for impetigo to develop.

See also ANTIBIOTIC MEDICATIONS; BLISTER; RASH; TINEA INFECTIONS.

ingrown hair A new HAIR that curls as it grows, slicing into the side of the hair follicle instead of arising from it to extend above the surface of the SKIN. An ingrown hair forms a painful red bump. The hair may grow its way through the wall of the follicle and above the skin, or may block the folli-

cle, causing INFLAMMATION and INFECTION (FOLLICULITIS). People who have curly or kinky hair are more likely to develop ingrown hairs. Men may develop ingrown hairs in the beard area as a consequence of shaving, sometimes called shaving bumps or shaving rash. ACNE and other inflammatory conditions of the skin that block the follicles can cause ingrown hairs. Moisturizing the skin helps open the follicles, allowing the hair to grow outward. Warm compresses can help release cells and sebum clogging the follicles, releasing the hair. Regular skin cleansing and mild exfoliants also help keep the follicles clear.

See also CARBUNCLE; DANDRUFF; FURUNCLE; PILONIDAL DISEASE; PSEUDOFOLLICULITIS BARBAE.

ingrown nail A toenail, or less commonly a fingernail, that grows beneath the surrounding SKIN. An ingrown nail, also called onychocryptosis, is painful and easily become infected. Often the tissue around the nail swells and grows over the nail (hypertrophy), further aggravating the site. Ingrown NAILS require medical attention and often minor surgery done in the provider's office. The provider injects the involved finger or toe with an anesthetic to numb it, then clips the corners of the ingrown nail to release it from the skin and trims away the excess tissue. Typically the doctor then applies a caustic solution, usually an acid preparation, to prevent the portion of nail from regrowing.

Tight-fitting shoes are a common cause of ingrown toenails. The shape of the toes also is a factor, with nails that have a pronounced curve being more likely to grow into the side of the toe. A common but ineffective home remedy for ingrown toenails is to cut a "V" into the top edge of the nail with the presumption that doing so will draw the edges of the nail away from the skin as the nail grows. The shape of the nail bed determines the growth pattern of the nail, however. The jagged edges that result at the top of the nail from this method present the potential for tears and snags that can separate the nail from the toe, another painful problem.

In some people ingrown nails tend to recur and may require more aggressive treatment such as removal of additional nail or the entire nail. Most people experience permanent relief after a single treatment to remove the edges of the nail. Podiatrists recommend trimming the nails straight across, with a slight margin over the edge of the toe. People who have DIABETES, PERIPHERAL VASCULAR DISEASE (PVD), or other conditions that impair blood circulation to the feet should inspect their feet daily and see a doctor or podiatrist regularly as well as at the first indication of irritation.

See also CORNS; PARONYCHIA.

jock itch See TINEA INFECTIONS.

K

Kaposi's sarcoma A CANCER that develops in the connective tissues that support the SKIN, with characteristic lesions on the skin and mucous membranes. There are several types of Kaposi's sarcoma. The two that are most common in the United States are AIDS-related Kaposi's sarcoma and transplant-related Kaposi's sarcoma.

In 1994 researchers discovered that human herpesvirus 8 (HHV-8), sometimes called Kaposi's sarcoma–associated herpesvirus (KSHV), causes Kaposi's sarcoma. However, the path of transmission remains uncertain. Like other herpesvirus strains, HHV-8 can remain dormant in the body for years without manifesting symptoms. A healthy IMMUNE SYSTEM seems to hold HHV-8 in check, preventing it from causing disease. Prolonged compromise of immune function, through conditions such as HIV/AIDS or through IMMUNOSUPPRESSIVE THERAPY such as occurs following ORGAN TRANSPLANTATION, allows HHV-8 to replicate (reproduce itself by taking over healthy cells) and cause Kaposi's sarcoma.

AIDS-related Kaposi's sarcoma Nearly all Kaposi's sarcoma in the United States occurs in people, predominantly men, who have AIDS. Doctors consider the appearance of Kaposi's sarcoma a defining sign that INFECTION with HIV (human immunodeficiency virus) has progressed to the disease state of AIDS. The activation of both HIV and HHV-8 may occur simultaneously, when both are present. Advances in treatment options for HIV/AIDS, notably highly active antiretroviral therapy (HAART), delay the progression of HIV to AIDS and consequently the appearance of Kaposi's sarcoma. About 6 percent of men with HIV/AIDS who receive HAART develop Kaposi's sarcoma, compared to 20 percent among those who do not.

Transplant-related Kaposi's sarcoma People who undergo organ transplantation typically receive immunosuppressive therapy, to prevent organ rejection, for the rest of their lives. The development of Kaposi's sarcoma arises from the immunosuppression, not the organ transplantation. The American Cancer Society estimates that about 1 in 200 transplant recipients taking immunosuppressive therapy to prevent organ rejection develop Kaposi's sarcoma. People who take long-term immunosuppressive therapy for other health conditions are also at risk for Kaposi's sarcoma.

Symptoms and Diagnostic Path

The key symptom of Kaposi's sarcoma is the presence of its characteristic lesions, which are nodular and raised, in people with long-term immunosuppression or who are HIV-positive. The lesions start as small, raised areas and are most common on the face, lower legs and feet, and genitals, though can develop anywhere on the body. They are usually darkly pigmented, often brownish red or purple, and sometimes itch. As they grow, the lesions may block the flow of blood or lymph, causing painful swelling. Lesions sometimes develop within the connective tissues of internal organs such as the LUNGS, where they can cause difficulty BREATHING, or the intestines, where they can cause GASTROINTESTINAL BLEEDING and ILEUS (intestinal obstruction).

The doctor can usually make a definitive diagnosis of Kaposi's sarcoma on the basis of visible lesions and immune or HIV status, with biopsy of a representative lesion to confirm the diagnosis if necessary. A chest X-ray can determine the presence of lesions in the LUNGS. Other imaging studies such as COMPUTED TOMOGRAPHY (CT) SCAN and

ENDOSCOPY can determine whether there are lesions elsewhere in the body, such as in the gastrointestinal tract, when symptoms suggest or the doctor suspects this is the case.

Treatment Options and Outlook

Treatment depends to some extent on whether the Kaposi's sarcoma is AIDS related or transplant related. In either form, methods to remove or reduce the lesions for improved comfort and appearance. Such methods may include

- localized CHEMOTHERAPY (injecting a cytotoxic agent directly into the lesion)
- external-beam RADIATION THERAPY that narrowly targets the lesion
- the topical retinoid preparation alitretinoin (Panretin) applied to the lesion
- surgery to reduce or excise (cut out) the lesion
- liquid nitrogen or cryotherapy, which freezes the lesion

Systemic chemotherapy reduces lesions in recurrent, widespread, or systemic (involving internal organs as well as the skin) disease in AIDS-related Kaposi's sarcoma, though it is not usually an option for transplant-related Kaposi's sarcoma because the immune system cannot withstand the assault. Treatment for Kaposi's sarcoma in people who have received organ transplants is often a delicate balance between suppressing enough immune function to stave off organ rejection and preserving enough immune response to fight INFECTION. Sometimes changing the immunosuppressive agent gives the immune system enough of a boost to fight the lesions, causing them to retreat or disappear.

SYSTEMIC CHEMOTHERAPY AGENTS TO TREAT AIDS-RELATED KAPOSI'S SARCOMA

daunorubicin (DaunoXome)	doxorubicin (Doxil)	paclitaxel (Taxol)

For most cancers, doctors apply an algorithm of symptoms and progression that helps determine effective treatment options and prognosis (potential for improvement). Kaposi's sarcoma occurs nearly always in circumstances of depressed or suppressed immune system function, skewing the conventional cancer-staging algorithms. The AIDS Clinical Trials Group (ACTG) system is the most commonly used staging algorithm for Kaposi's sarcoma associated with AIDS or transplant-related immunosuppression. The ACTG system assesses three factors:

- number of lesions
- CD4 cell count, which represents immune system function
- systemic conditions that indicate compromised immune function

Each factor receives a rating of zero (good) or one (poor), reflecting the likelihood for five-year survival, a standard prognosis marker for cancer. Kaposi's sarcoma of the skin is seldom itself fatal, though the extent of its presence indicates the immune system cannot protect the body from infection. Kaposi's sarcoma of internal organs can be fatal. This cancer is not curable in AIDS or active immunosuppressive therapy, so treatment aims to relieve symptoms.

Risk Factors and Preventive Measures

In the United States, HIV infection is the leading risk factor for Kaposi's sarcoma. Methods to reduce exposure to HIV/AIDS also reduce the risk for Kaposi's sarcoma. Most AIDS-related Kaposi's sarcoma occurs in men who have sex with men, leading researchers to postulate that there is a route of sexual transmission for HHV-8. Safer sex practices are crucial.

As a result of the growing availability and acceptance of organ transplantation, the number of cases of Kaposi's sarcoma among transplant recipients is steadily rising. The risk increases the longer the person receives immunosuppressive therapy. Newer immunosuppressive agents more selectively target the immune functions responsible for organ rejection, leaving other immune functions undisturbed.

See also CANCER TREATMENT OPTIONS AND DECISIONS; HIV/AIDS PREVENTION; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SEXUALLY TRANSMITTED DISEASES (STDS); STAGING AND GRADING OF CANCER; VIRUS.

keloid An overgrowth of collagen after a wound has finished HEALING. A keloid typically forms as folds or bunches of tissue. Keloids are fibrous, spongy in consistency, and often dark red. They form most often on the earlobes, upper chest, and shoulders though can develop anywhere on the body. Keloids are more common in people who have dark skin, and in people under age 50. Though keloids do not present any health problems, they can become irritated from rubbing on clothing. A corticosteroid medication injected into the keloid often halts its growth and causes the existing excess tissue to recede. The dermatologist can surgically remove large keloids or keloids that recur.

See also ACROCHORDON; CORTICOSTEROID MEDICATIONS; SCAR.

keratinocyte The cell type that makes up most of the epidermis, also called a squamous cell. Keratinocytes originate in the first of the four layers of the epidermis, the stratum basale. Here they either replicate to generate new keratinocytes or migrate upward. Migratory keratinocytes acquire melanin from melanocytes. The keratinocytes carry this pigment to the outer layers of the SKIN, where it appears as the skin's normal color or causes the skin to darken (as in a tan). At each of the epidermis's layers the keratinocytes become more compressed. Their internal structures break down, and the keratin they contain causes them to harden.

At the stratum corneum, the outer layer of the epidermis, the keratinocytes overlap tightly, looking somewhat like irregular shingles when viewed under the microscope. At the culmination of this journey, which takes about four weeks, the keratinocytes die and slough from the skin's surface. The fingernails and toenails are much more tightly compressed and hardened keratinocytes. They do not shed as does the stratum corneum but instead grow forward over the front of the fingers and toes at the rate of about one eighth inch every four to five weeks.

Hyperkeratosis is a state in which the keratinocytes migrate through the epidermis far more rapidly than normal, sometimes cutting the journey to 10 days. This accelerated journey causes more keratinocytes than the body can shed to accumulate in the HAIR follicles and sebaceous structures, causing numerous hyperkeratosis-related conditions from ACNE and atopic DERMATITIS to PSORIASIS and SEBORRHEIC KERATOSIS. Squamous cell carcinoma, a common type of SKIN CANCER, arises from keratinocytes.

For further discussion of keratinocytes within the context of integumentary structure and function please see the overview section "The Integumentary System."

See also ICHTYOSIS; MELANOCYTE; NAILS.

keratoacanthoma A form of squamous cell carcinoma (SKIN CANCER) that appears suddenly and grows rapidly, though has a low rate of METASTASIS (spreading). Like other forms of skin CANCER, keratoacanthoma is the consequence of extensive sun exposure that manifests decades later. Researchers have identified a number of chromosomal abnormalities that appear connected with keratoacanthoma, suggesting a strong genetic component or familial predisposition (tendency of the cancer to run in families).

Most keratoacanthomas develop in people over age 50, though may occur at younger ages in people who are taking IMMUNOSUPPRESSIVE THERAPY (such as following ORGAN TRANSPLANTATION) or who are IMMUNOCOMPROMISED. A keratoacanthoma lesion typically develops on skin surfaces that receive or have received significant sun exposure and may initially appear to be a FURUNCLE (boil) or a cyst. The lesion often appears to heal, though seems to take a long time to do so (up to a year).

Though it appears that keratoacanthoma eventually resolves (heals) on its own, the risk that the lesion could instead be squamous cell carcinoma or that the keratoacanthoma could metastasize causes dermatologists to recommend immediate removal with microscopic examination to confirm the diagnosis. Keratoacanthomas tend to recur. The dermatologist may recommend surgical removal of the lesion or inject it with a chemotherapeutic agent, either of which generally is adequate treatment.

See also ACTINIC KERATOSIS; CANCER TREATMENT OPTIONS AND DECISIONS; SKIN SELF-EXAMINATION.

keratosis pilaris A very common condition in which the keratocytes produce excessive keratin, clogging the HAIR follicles and forming small

bumps on the SKIN that resemble GOOSE BUMPS. The bumps may be the same color as the skin or slightly reddened and create a texture like rough sandpaper on the skin's surface. Occasionally the bumps itch. Keratosis pilaris most often affects the lower arms and inner thighs, though can occur anywhere on the body, and is most common among adolescents. Researchers have implicated number of gene mutations for keratosis pilaris.

The eruption and pattern of bumps present a fairly conclusive diagnostic picture. A biopsy can confirm any questionable presentations. Treatment typically consists of measures to increase exfoliation, which clears accumulated cells from the hair follicles. Topical products containing alphahydroxy acids such as lactic acid are often helpful. The dermatologist may prescribe a topical retinoid medication to treat resistant symptoms. Keratosis pilaris becomes increasingly uncommon with age and generally resolves by the early 20s.

See also ACNE; DERMATITIS; ICHTHYOSIS; KERATOCYTE; MUTATION; PITYRIASIS ROSACEA.

L

laser skin resurfacing A method for smoothing scars, ACNE pitting, WRINKLES, and other blemishes from the SKIN, primarily on the face, using a heat (usually carbon dioxide) laser. The laser focuses a high-intensity beam of light that the dermatologist moves across the surface of the skin, precisely targeting the depth and skin areas for resurfacing. This precision control allows the dermatologist to target some areas more deeply than others, accommodating such variations in the skin as fine wrinkles to moderate scars. Like CHEMICAL PEEL and DERMABRASION, laser skin resurfacing achieves skin smoothing by destroying layers of cells. The new skin that grows to replace the destroyed skin is tight and smooth.

The dermatologist performs laser skin resurfacing as an AMBULATORY SURGERY procedure in a clinic, office facility, or an ambulatory surgery facility, typically using local anesthetic to numb the skin and a sedative medication for relaxation and improved comfort. The length of time the procedure requires depends on what kinds of blemishes the dermatologist is treating. The dermatologist may cover the treated surfaces with an ointment and bandages, which remain in place for one or two days.

After the procedure the treated skin surfaces are red, swollen, and tender or painful. After a day or two the skin scabs or crusts, a normal stage in the HEALING process. The dermatologist removes any bandages at this time. As the skin heals the scabs fall away, typically in 10 to 14 days. The new skin is red and shiny, transitioning to normal pigmentation and texture over the following six to eight weeks (though most of the redness subsides in about three weeks). Full HEALING and noticeable improvement take about six months.

The risks of laser skin resurfacing are slight and include excessive bleeding, INFECTION, and pigmentation changes. As with all cosmetic procedures, it is important to fully understand what laser skin resurfacing can and cannot accomplish. Most people who receive treatment from a qualified dermatologist or plastic surgeon are satisfied with the results. Some people may find that the new skin is sensitive to soaps, cleansers, and makeup used before the procedure.

The new skin is very vulnerable to damage from the sun during as well as after healing, requiring protective clothing, such as a wide-brimmed hat or scarf, and high sun protection factor (SPF) sunscreen whenever sun exposure is necessary. The effects of laser skin resurfacing typically last several years, with wrinkles gradually returning as a normal function of the aging process. Alterations such as SCAR revision or removal are permanent.

See also AGING, INTEGUMENTARY CHANGES THAT OCCUR WITH; BOTULINUM THERAPY; LASER SURGERY; SUN PROTECTION; SURGERY BENEFIT AND RISK ASSESSMENT.

lentigines Dark spots of varying size on the SKIN, also called freckles, liver spots, or age spots. Lentigines develop as a result of continued sun exposure and indicate damage to the skin. A single spot is a lentigo. Lentigines are often widespread on areas of skin that receive high sun exposure, such as the face and arms, sometimes covering the entire surface of exposed skin. It is important to examine the skin in areas of heavy sun damage, such as those with many lentigines, for signs of SKIN CANCER as most skin cancer arises from such damage.

Cosmetic products such as creams and lotions containing alphahydroxy acid, lactic acid, or other mild fruit acids can lighten lentigines, functioning as a mild CHEMICAL PEEL. These products have a

mild bleaching action that reduces pigmentation in the areas of application. Cosmetic procedures such as dermatologist-performed chemical peel, hydroquinone application (a bleaching agent), or LASER SURGERY can diminish or eliminate lentigines and other blemishes on the face.

See also SKIN SELF-EXAMINATION; SUNBURN; SUN PROTECTION.

lesion A generalized term for any abnormal growth. Lesions can result from injury, disease, or surgery. Some lesions are malignant (cancerous) though most lesions are benign (noncancerous). Numerous types of lesions affect the SKIN. Their characteristics help define and diagnose disorders and conditions of the skin as well as systemic disorders that manifest dermatologic symptoms.

COMMON TYPES OF SKIN LESIONS

ACHROCHORDON	ANGIOMA	basal cell carcinoma
BIRTHMARK	BLISTER	
BULLA	DERMATOFIBROSIS	KELOID
LENTIGINES	MACULE	malignant melanoma
NEVUS	NODULE	
PAPILLOMA	PAPULE	plaque
PUSTULE	SCALE	SCAR
squamous cell carcinoma	TELANGIECTASIS	ulcer
	VESICLE	WHEAL

See also DERMATITIS; PLAQUE, SKIN; PSORIASIS; RASH; SKIN CANCER.

lice See PEDICULOSIS.

lichen planus A common condition affecting the SKIN that appears as small, shiny, reddish purple (violaceous) bumps that itch, sometimes intensely. The bumps grow together in a scalelike pattern that resembles tree lichen. Lichen planus nearly always occurs in adults.

Symptoms and Diagnostic Path

Lichen planus typically erupts on the inner surfaces of the lower arms and wrists, along the shins and inner ankles, and along the lower back. Occasionally lichen planus appears on the scalp, where it can cause temporary or permanent ALOPECIA (hair loss), or affects the fingernails and toenails, causing ridges and grooves. In the MOUTH, lichen planus is light in color and the scaling more diffuse, creating a lacelike pattern lighter in color than the surrounding mucosa. The distinctive color and pattern of the RASH allow the dermatologist to make a quick diagnosis. The doctor may biopsy lichen planus lesions that appear in the mouth, as they resemble other conditions (such as CANDIDIASIS and precancerous lesions) that require different treatment.

Treatment Options and Outlook

Outbreaks of lichen planus typically retreat without medical intervention, though ANTIHISTAMINE MEDICATIONS and topical CORTICOSTEROID MEDICATIONS can help relieve the itching. In severe cases, the dermatologist may prescribe oral corticosteroids such as prednisone to suppress the IMMUNE RESPONSE. An outbreak may last several weeks to several months and typically flares in irregular recurrences over a period of years. Gentle, regular skin cleansing and moisturizing can help to manage and reduce symptoms.

Risk Factors and Preventive Measures

Dermatologists do not know what causes lichen planus, though believe it is an immune response of some sort, either an autoimmune condition or an immune response to a VIRUS, likely with a genetic predisposition. Lichen planus also occurs in HEPATITIS C INFECTION, is an early sign of transplant organ rejection, and is a rare SIDE EFFECT of some medications such as long-term therapy with the antimalarial medication quinidine and some NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) used for OSTEOARTHRITIS. Avoiding exposure to substances that can cause lichen planus, when identified, usually prevents future outbreaks though some people continue to experience cycles of the condition for several years.

See also AUTOIMMUNE DISORDERS; DERMATITIS; ICHTHYOSIS; LESION; LEUKOPLAKIA; LICHEN SIMPLEX CHRONICUS; PRURITUS; PSORIASIS.

lichen simplex chronicus A SKIN condition, sometimes called neurodermatitis, in which an itchy RASH erupts in response to continued scratching of the skin. Over time, the involved areas develop hyperkeratosis, an overgrowth of keratinocytes that gives the areas a scaly, lichen-

like appearance (plaques). Lichen simplex chronicus sometimes develops in areas of the skin that have previously had irritation, such as from DERMATITIS or abrasive injury, or frequently irritated, such as from clothing that rubs or constricts. Stress and strong emotional responses exacerbate the rash and the itching. The condition appears more common in people who have DEPRESSION or anxiety, hence the former term, neurodermatitis, for the condition. Most often, however, there is no clear cause for the condition.

Symptoms and Diagnostic Path

The rash of lichen simplex chronicus begins with small reddened areas (macules) that itch, commonly forming on the neck and the inner surfaces of the arms and legs. Most people who have lichen simplex chronicus describe the itching as intense, such that they are unable to stop scratching. With scratching, the rash becomes more extensive. Many people find the itching more pronounced at night before sleep, creating difficulty falling asleep or staying asleep. The dermatologist typically diagnoses lichen simplex chronicus on the presentation of these symptoms, though may choose to biopsy questionable lesions to confirm the diagnosis.

Treatment Options and Outlook

Treatment targets relieving the symptoms, primarily the itching. The dermatologist may prescribe oral ANTIHISTAMINE MEDICATIONS and topical CORTICOSTEROID MEDICATIONS, which work together to mitigate the IMMUNE SYSTEM's response to the persistent irritation scratching causes. Antihistamine medications are especially helpful at bedtime, when many people find the itching most intense, as they tend to cause drowsiness. Some people benefit from ANTIANXIETY MEDICATIONS. Methods such as VISUALIZATION, BIOFEEDBACK, and ACUPUNCTURE may help. Mild to moderate lichen simplex chronicus generally heals without residual effects, though more severe manifestations may leave scarring and altered pigmentation (either lighter or darker patches of skin in the sites of the healed plaques).

Risk Factors and Preventive Measures

The causes of lichen simplex chronicus remain elusive. Dermatologists disagree on whether the rash or the itching appears first, though the end result is that the rash itches and continued scratching perpetuates the rash. The most important factor is to avoid scratching, as persistent scratching causes other damage to the skin that increases the risk for INFECTION and scarring. In many people, episodes follow stressful experiences. Stress management techniques and relaxation methods provide other means for diffusing the physiologic effects of stress.

See also GENERALIZED ANXIETY DISORDER (GAD); ICHTHYOSIS; KERATINOCYTE; LESION; LICHEN PLANUS; MACULE; PLAQUE, SKIN; PRURITUS; PSORIASIS; SCAR; STRESS AND STRESS MANAGEMENT.

M

macule A small SKIN LESION that is flat, smooth, and discolored. Macules are common and may appear as the presenting symptom for numerous dermatologic and other health conditions. Often the only symptom they present themselves is discoloration, though some macules itch or hurt. The discoloration may be hyperpigmentation (darker than the surrounding skin) or hypopigmentation (lighter than the surrounding skin). A macule is the same texture and thickness as the adjacent skin and generally no larger than two inches in length, width, or diameter. The most common macule is a lentigo, or freckle.

See also BIRTHMARK; LENTIGINES; NODULE; PAPULE; PUSTULE; VITILIGO.

malignant melanoma See SKIN CANCER.

melanocyte A type of cell prominent in the dermis (middle layer of the SKIN) that produces melanin, the pigment that gives color to the skin as well as protects the skin from ultraviolet light damage. There are two types of melanin: the dark brown pigment eumelanin and the red/yellow pigment pheomelanin. The skin contains the same number of melanocytes no matter what the individual's natural skin color. The melanocytes in darker skin are more active than those in lighter skin. The eyes and HAIR also contain melanocytes.

Melanogenesis

The exclusive role of melanocytes is to produce melanin (melanogenesis), a somewhat sequential process. To prepare for melanogenesis, the body produces the enzyme tyrosinase. Genetic encoding regulates this process. Tyrosinase initiates conversion of the amino acid tyrosine, which the body synthesizes from dietary proteins such as meats and which the melanocytes store, into dopaquinone. The dopaquinone forms the pigments eumelanin and pheomelanin, which collectively comprise mel-anin.

Exposure to ultraviolet light, notably sunlight, initiates a sequence of hormonal and chemical events that stimulate melanocytes to produce melanin (melanogenesis):

1. Sunlight (or other ultraviolet light exposure) damages the cells of the skin. The damage activates the natural repair mechanisms within the cells, which releases chemicals into the bloodstream that travel to the PITUITARY GLAND.
2. In response the pituitary gland releases melanocyte-stimulating hormone (MSH), to bind with melanocytes.
3. Melanocytes pass packets of melanin molecules to the keratocytes, which carry them to the outer layer of the epidermis as they migrate upward.

The resulting skin color depends on the mix of eumelanin and pheomelanin the melanin contains. The melanin in light skin contains more pheomelanin than eumelanin. In darker skin the balance tips the other way with the melanin in dark skin containing more eumelanin than pheomelanin. In the epidermis, melanin protects the skin from damage by absorbing ultraviolet light. The darker the skin, the less ultraviolet light penetrates the epidermis. In general, it takes about a week of regular sun exposure to generate a tan adequate to begin protecting the skin from further sun damage, though the tan itself signals sun damage.

Dysfunctions of Melanocytes

There are three significant dysfunctions of melanocytes:

- ALBINISM is a deficit or absence of pigmentation (hypopigmentation) caused by a MUTATION in the genetic encoding for tyrosinase. The body may produce little or none of this enzyme, reducing or completely blocking melanogenesis. The dermatologic consequence is extremely light-colored skin that cannot protect itself from ultraviolet light damage.
- VITILIGO is a hypopigmentation disorder of autoimmune origin in which the melanocytes in areas of the skin die, leaving the skin without pigmentation.
- Malignant melanoma is a serious type of SKIN CANCER that arises from melanocytes.

For further discussion of melanocytes within the context of integumentary structure and function, please see the overview section, "The Integumentary System".

See also AMINO ACIDS; KERATINOCYTE; PHENYLKETONURIA (PKU).

melasma See CHLOASMA.

miliaria Small bumps that form on the SKIN in environmental conditions of high heat and humidity, when the body produces much sweat that cannot evaporate and instead pools on the surface of the skin. The bumps may be red (miliaria rubra) or clear and filled with fluid (miliaria crystallina). Clothing may further inhibit sweat evaporation. The pooling creates irritation and INFLAMMATION that obstructs the sweat glands. Most miliaria, commonly called heat RASH, improves with self-care to cool the body, which causes the SWEAT GLANDS to decrease production. The skin bumps generally go away in three to five days. Newborns are particularly susceptible to miliaria in the first week or two of life. Miliaria also sometimes occurs in people who have high fevers.

See also HEAT EXHAUSTION; HEAT STROKE; HYPERTHERMIA.

Mohs' micrographic surgery A specialized technique for removing certain skin cancers such as basal cell carcinomas and squamous cell carcinomas. In an outpatient OPERATION (AMBULATORY SURGERY) with local anesthetic and a sedative for relaxation if necessary, the dermatologist removes one thin layer of the tumor at a time and examines each specially stained layer under the microscope. The surgery continues until the tissue sample shows a one- to two-millimeter margin of healthy tissue on all borders, ensuring that the dermatologist removes all of the malignancy. Because Mohs' micrographic surgery is so precise it removes only the malignancy, sparing as much surrounding tissue as possible.

By comparison, conventional excision removes the tumor and what the surgeon believes is a reasonable amount of surrounding tissue to provide clean margins, which can result in removing considerably more tissue than just the malignancy. A pathologist later examines frozen sections of the tissue to confirm the margins. With conventional excision there is a change that the margins could be positive (contain cancer cells) and the surgeon would have to do another operation to remove more tissue.

Dermatologists use Mohs' micrographic surgery when the SKIN CANCER is on the face, nose, eyelids, or around the mouth, or if it is a larger, more aggressive cancer on the body. The procedure may take several hours altogether to complete, depending on how many layers of tissue the dermatologist must remove to get clean margins. Many cancers removed using Mohs' micrographic surgery heal with minimal scarring. The dermatologist performing the surgery usually repairs any residual defect as dermatologists also perform reconstructive surgery. Mohs' micrographic surgery has an overall cure rate of 95 percent and up to 99 percent for certain kinds of malignant lesions, the highest for all current forms of treatment for these two types of skin cancer. Frederic E. Mohs, M.D. (1910–2002), discovered the technique while a medical student in the 1930s.

See also CANCER TREATMENT OPTIONS AND DECISIONS; LESION; SURGERY BENEFIT AND RISK ASSESSMENT.

mole See NEVUS.

nails The hardened epidermal layer covering the top surfaces of the tips of the fingers and toes. Nails are made of cornified, compacted SKIN cells (keratinocytes) that grow from the base of the nail (matrix or nail-bed root). Though the cells of the matrix are alive, the cells that make up the nails are dead. New cell growth from the matrix pushes the nail outward across the tip of the finger or toe. In adults the fingernails grow about two tenths inch in a week. The cells the matrix produces today will reach the end of the finger in about six months.

Like the skin, the nails provide insights into the overall health situation of an individual. Certain changes in the nails signal specific health conditions. Such characteristics include

- banding: stripes of dark or light across the width of the nail bed, visible through the nail

HEALTH IMPLICATIONS OF NAIL CHARACTERISTICS

Nail Characteristic	Possible Health Implications
Beau's lines	serious injury or illness that disrupts nail growth
clubbing	chronic pulmonary conditions, HEART FAILURE, low blood oxygen levels
dark band at tops of nails, bottoms of nails normal color (Terry's nails)	age, CANCER, congestive heart failure, DIABETES, CIRRHOSIS, HYPERTHYROIDISM
koilonychia	iron-deficiency ANEMIA
leukonychia	arsenic poisoning, mineral deficiency, trauma to the nail matrix
onycholysis	thyroid disease, fungal INFECTION, PSORIASIS, adverse DRUG reaction
PETECHIAE (pinpoint hemorrhages)	ENDOCARDITIS, THROMBOCYTOPENIA, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
stippling	psoriasis, ALOPECIA AREATA, injury to the nail
white band at the bottoms of nails, tops of nails normal color (half-and-half nails)	UREMIA, KIDNEY failure
yellow nail syndrome (yellow-green discoloration consistent through all nails)	chronic pulmonary disorders such as BRONCHITIS and EMPHYSEMA, NICOTINE staining

- Beau's lines: indentations in the nail surface that extend across the width of all the nails at about the same position on each
- clubbing: end of the finger or toe becomes enlarged and the angle between the nail fold and the nail plate exceeds 180 degrees
- discoloration: may be widespread throughout the nail or occur in spots or streaks
- koilonychia: nails soften and the edges rise, leaving a large spoonlike indentation in the center of the nail
- leukonychia: white spots or streaks in the nail
- onycholysis: separation of the nail from the nail bed
- PETECHIAE: red or dark spots beneath the nail
- stippling: the formation of small pits in the surface of the nail

For further discussion of the nails within the context of integumentary structure and function please see the overview section "The Integumentary System."

See also INGROWN NAIL; KERATINOCYTE; ONYCHOMYCOSIS.

neurodermatitis See LICHEN SIMPLEX CHRONICUS.

nevus A discolored LESION on the SKIN. Nevi are very common and may take various shapes and colors. Most nevi contain primarily melanocytes and may differ in texture from the surrounding skin. A nevus may be smooth, distinguishable only by its color, or rough and segmented. Some nevi contain coarse HAIR. The most common form of nevus is a mole, a small lesion that can be smooth or raised and is usually darker in color than the surrounding skin. A nevus may be congenital (present at birth) or acquired (develops at any point in the lifespan after birth). Nearly everyone has some nevi by early adulthood.

Giant congenital nevus, a rare presentation of congenital nevus, may cover a large area of the skin's surface. In another uncommon genetic disorder, neurocutaneous melanosis, nevi develop within the structures of the BRAIN and SPINAL CORD. The presence of melanocytes in some NERVOUS SYSTEM tissue is normal and functional. Melanocytes populate the substantia nigra, for example, a structure of the midbrain. The pigmented cells of substantia nigra produce dopamine, a NEUROTRANSMITTER essential for the brain's coordination of MUSCLE function throughout the body. However, melanocytes in other parts of the nervous system can generate overgrowths—nevi—just as they do on the skin. Such nevi cause pressure as they grow, resulting in neurologic symptoms.

Acquired nevi begin to appear during childhood in most people, with the most intense activity occurring in middle adulthood (ages 30 to 50). Though sun exposure plays a role in their development, genetic encoding seems to regulate characteristics such as size, color, shape, and numbers. In the typical structure of the dermis, the layer of skin where melanocytes reside in greatest concentration, melanocytes are frequent but are not in contact with each other. Researchers believe this distribution pattern results from "contact inhibition" genetic encoding. A nevus can form when the contact inhibition lapses, allowing the melanocytes to drift into contact with one another. Sometimes nevi appear after extensive injury to the skin, such as occurs with conditions that cause widespread blistering. This suggests that such injuries disrupt contact inhibition in some way, though the mechanisms through which this occurs remain unknown.

A nevus should have regular borders, consistent coloration, and a symmetrical (balanced) appearance. A doctor should evaluate a nevus that has or develops irregular borders, variable coloration, or an asymmetrical appearance as these characteristics may indicate a nevus that is becoming cancerous.

Though nevi are themselves benign (noncancerous), they can become cancerous over time and particularly with repeated, unprotected sun exposure. Congenital nevi in particular carry an increased risk for malignant melanoma, a serious type of SKIN CANCER. Most often, the only health concerns with nevi are the increased risk for malignancy and cosmetic appearance. The dermatologist may choose to remove nevi that receive frequent irritation, such as those that form in

areas where clothing rubs them. The resulting SCAR may require PLASTIC SURGERY for the desired cosmetic appearance, depending on the size, nature, and location of the nevus. Small nevi heal without noticeable scarring. Nevi do tend to recur after removal.

See also GENETIC DISORDERS; MELANOCYTE; PARKINSON'S DISEASE; SKIN SELF-EXAMINATION; VITILIGO.

nodule A small cluster of cells that arises from the subcutaneous or dermis layer of the SKIN and forms a swelling. Nodules are solid and distinct from the surrounding tissue. Most skin nodules arise from causes other than dermatologic, such as neurofibroma and LIPOMA. Nodules may exist in other parts of the body, typically as symptoms of systemic disease.

See also MACULE; PAPULE; PUSTULE.

onychomycosis A common fungal INFECTION, typically CANDIDIASIS or TINEA, of the fingernail or toenail. The infection causes the nail to thicken, discolor, fragment, and peel or crack. Though some people experience itching, PAIN, or other discomfort with onychomycosis, most people seek medical care because of the nail's appearance. Onychomycosis affects the structure and function of the nail, however. Onychomycosis affecting multiple toenails can interfere with proper walking, and onychomycosis of the fingernails may reduce gripping ability and the ability to perform tasks such as typing or keyboarding. The doctor often can make the diagnosis based on the appearance of the NAILS, though may choose to examine tissue samples under the microscope to confirm the presence of the infective FUNGUS.

Eradication of the fungus often requires oral antifungal medication in combination with topical antifungal medication. Onychomycosis can be a stubborn infection, making several courses of treatment necessary. Early diagnosis and treatment affords the most successful results.

See also ANTIFUNGAL MEDICATIONS; INGROWN NAIL; PARONYCHIA; PSORIASIS.

P

papilloma A general classification of tumors arising from the epidermis (outer layer of the SKIN) as well as the epithelial layer of the mucous membranes. Warts, HUMAN PAPILLOMAVIRUS (HPV) lesions (also called condylomata or genital warts), and POLYPS are papillomas. Though papillomas are noncancerous (benign), some types of papillomas, notably intestinal polyps, are the foundation for certain cancers. Doctors generally remove polyps and treat HPV infections and lesions because these are among the papillomas that can become cancerous. Many people prefer to have common warts removed for cosmetic purposes. Irritation such as from clothing that rubs or frequent trauma can cause papillomas to bleed.

See also ACROCHORDON; ADENOCARCINOMA; ADENOMA-TO-CARCINOMA TRANSITION; COLORECTAL CANCER; INFECTION; LESION; WART.

papule A small, raised bump arising from the epidermis that is distinctive and firm to the touch. Papules may be discolored or the same color as the surrounding SKIN. The presence of papules is a symptom of many dermatologic and other health conditions. Papules that cluster together form a skin plaque, usually taking on a hardened, flaky appearance.

See also MACULE; NODULE; PLAQUE, SKIN; PUSTULE.

paronychia INFLAMMATION and INFECTION of the SKIN that surrounds the NAILS. Paronychia commonly occurs in people who bite their fingernails or the skin around them or who have frequent cuts around their fingernails. Paronychia is common in children who suck their thumbs or fingers. Paronychia of a toenail may accompany an ingrown toenail. Splinters, INSECT BITES AND STINGS, and other injuries around the tips of the fingers or toes can fester, allowing infection to creep under the nail.

Paronychia can be acute (come on suddenly) or chronic (persist or recur over a period of time). Acute paronychia is generally painful and pustular (produces pus). *Staphylococcus aureus,* a strain of BACTERIA that normally lives on the skin, is the usual cause of the infection. Less commonly, a strain of *Streptococcus* or *Pseudomonas* (bacteria), or the FUNGUS (yeast) *Candida albicans,* may be the culprit.

Symptoms of paronychia include redness, swelling, PAIN, and occasionally bleeding or pus discharge. The doctor can diagnosis paronychia based on the symptoms and the history of their development and occurrence. Treatment may include

- warm soaks three to four times a day, keeping the affected finger or toe dry at all other times
- topical antibiotic or ANTIFUNGAL MEDICATION
- oral antibiotic or antifungal medication

Occasionally the doctor may need to lance (make a sterile incision) the infected area to release the pus collected within. The paronychia generally heals within 7 to 10 days, though may recur if related to behaviors or exposures that continue. Untreated paronychia becomes very painful and may cause infection to spread into deeper tissues, with the potential for permanent damage to the nail as well as to tendons, ligaments, MUSCLE, and BONE.

See also CELLULITIS; INGROWN NAIL; OSTEOMYELITIS; WHITLOW.

pediculosis Infestation with lice, parasites that live on the SKIN and feed by sucking BLOOD through

CHARACTERISTICS OF PARONYCHIA

	Acute	Chronic
symptoms	PAIN, redness, and swelling SKIN around the nail appears tight and bright red may have pus precipitating trauma (sliver, pulled hangnail, biting the nail or skin) sudden onset	tenderness and swelling of the skin around the nail redness and increased discomfort with prolonged exposure to water (such as washing dishes) ongoing for longer than four to six weeks repeated exposure to water, chemicals, other irritants discolored or thick nail on the affected finger or toe separation of the cuticle from the nail bed
infective agent	*Staphylococcus aureus* *Streptococcus* *Pseudomonas*	*Candida albicans*
medication	oral ANTIBIOTIC MEDICATIONS such as clindamycin, cephalexin, or amoxicillin and clavulanic acid	topical antifungal medication such as miconazole oral antifungal medication such as ketoconazole or fluconazole

small punctures they make through the skin. Lice attach their eggs, called nits, to HAIR shafts. Of the numerous species of lice, three afflict humans:

- *Pediculus humanus capitis*, which infests the scalp
- *Pediculus humanus corporis*, which infests the body
- *Pediculus pubis*, which infests the pubic region

Each species has unique claw and MOUTH structures that allow survival in the particular region of the body, and each species can infest only the body region for which it is adapted. However, infestation with two or more species is common. *Pediculosis* refers collectively to infestation with any species of lice, and affects around 12 million Americans each year.

Pediculosis spreads easily through direct and indirect contact, and is so common among school-age children that schools routinely screen for its presence. Crowded environments, such as schools and dormitories, allow close contact between people, permitting the lice to spread from one person to another. Pediculosis may be present for as long as two months before causing appreciable symptoms, increasing the potential for extending infestation. Head and pubic lice and nits resist the most scrupulous cleansing. Infrequent clothing changes are often a factor with body lice infestation. Poor PERSONAL HYGIENE such as infrequent bathing can allow secondary problems such as INFECTION to develop.

Symptoms and Diagnostic Path

The most common symptom of pediculosis is itching, which is often particularly intense at night when the lice feed. The saliva of the lice contains enzymes to delay coagulation (blood clotting) which irritate the skin. The bites leave reddened papules (raised bumps) that continue to itch. Finding nits (eggs attached to hair shafts) is the conclusive diagnostic marker. Nits are difficult to remove, which helps distinguish them from other matter that might collect on the skin or hair, as well as from conditions such as seborrheic DERMATITIS and common DANDRUFF. Examination with fluorescence (Woods lamp) causes the lice and nits to glow yellow or green.

Treatment Options and Outlook

Treatment for head or pubic infestation combines removing the nits with a fine-tooth comb (nit comb) and shampooing or washing with an insecticide-based product such as permethrin (Nix) or malathion (Ovid). Multiple treatments about a week apart for a month, or until no nits are present, are necessary to cover the lifespan of the louse, which is about 35 days. It is important to

carefully follow the label directions for the product and to leave the product on the hair or skin for the instructed length of time. Most treatment regimens include combing the hair with a nit comb after shampooing. All individuals in the household should receive treatment.

It is also necessary to wash clothing and bed linens in hot water (130°F or more) for at least five minutes, and placing stuffed toys in sealed plastic bags for two weeks. The hot water wash kills any lice or nits, and the plastic bag method deprives any lice or nits that hatch of nourishment. Because body lice live on the clothing rather than the skin, washing the clothing in hot water is usually adequate.

Risk Factors and Preventive Measures

Most pediculosis leaves no residual health consequences, although secondary infections may develop with excessive scratching. However, sexual contact generally transmits pubic pediculosis, which raises concern for SEXUALLY TRANSMITTED DISEASES (STDS). Body lice (*P. humanus corporis*) can carry serious bacterial diseases including typhus.

See also PAPULE; PARASITE; PUBLIC HEALTH CONCERNS OF INFECTIOUS DISEASES; SCABIES; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

pemphigus An autoimmune disorder in which large, painful bullae (blisters) form on the SKIN and mucous membranes. The bullae develop within the epidermis, the skin's uppermost layer, giving them a very thin surface. They rupture and tear easily, exposing the skin to INFECTION and interfering with the skin's ability to carry out its numerous functions. The ruptured bullae form crusts while they heal, though typically heal without scarring. Some forms of pemphigus can cover large portions of the skin's surface are potentially fatal. There are three main forms of pemphigus:

- pemphigus vulgaris, the most common form in which bullae develop in the MOUTH and under the eyelids as well as on the skin surfaces of the face, neck, chest, axillae (underarms), and groin
- pemphigus foliaceus, the mildest form in which bullae develop mostly on the skin of the scalp and face though sometimes involve the back and chest
- paraneoplastic pemphigus, which occurs only secondarily to CANCER and can involve the mucous membrane lining the ESOPHAGUS and airways (TRACHEA and bronchi)

Pemphigus occurs when antibodies the IMMUNE SYSTEM produces attack and destroy certain proteins on the surface of epidermal keratinocytes, the skin cells that make up the epidermis, causing them to separate from one another. The proteins are like glues that hold the keratinocytes together. Dermatologists do not know what causes pemphigus to develop as an autoimmune process, though occasionally it occurs as an ADVERSE REACTION to certain medications, notably penicillamine (taken to treat severe RHEUMATOID ARTHRITIS) and carbidopa/levodopa (taken to treat PARKINSON'S DISEASE).

Symptoms and Diagnostic Path

The primary symptom of pemphigus is the appearance of bullae that start as small blisters. In early outbreaks the blisters may rupture and heal without taking the characteristic bulla form. As outbreaks become more frequent and progressive, however, the blisters enlarge over several days to a week. In the early stages of the disorder's manifestation, the pattern and appearance of bullae may be similar to other autoimmune symptoms, notably the sores that can appear with HIV/AIDS. Biopsy of the lesions can help to rule out other causes.

The location and extent of the bullae characterizes the form of pemphigus. Pemphigus vulgaris typically begins with blisters in the mouth, with outbreaks quickly following on other skin surfaces as well as the mucous membranes lining the NOSE and the URETHRA. The bullae of paraneoplastic pemphigus, which only occurs in conjunction with cancer, also originate in the mouth though quickly involve the esophagus as well as the skin. Pemphigus foliaceus bullae are smaller and remain confined primarily to the head (scalp and face), and do not involve the mouth or other mucous membranes.

Treatment Options and Outlook

Treatment targets relief of symptoms during outbreaks and mitigation of future outbreaks to the extent possible. Treatment varies with the form and severity of pemphigus, though typically includes oral or injected CORTICOSTEROID MEDICATIONS along with oral ANALGESIC MEDICATIONS for PAIN relief and ANTIBIOTIC MEDICATIONS to treat infection when necessary. Severe outbreaks may require IMMUNOSUPPRESSIVE MEDICATIONS to subdue the IMMUNE RESPONSE, or PLASMAPHERESIS, a therapy that cleanses the blood's serum of antibodies. Cytotoxic drugs such as those used in CHEMOTHERAPY also improve symptoms in some people with severe outbreaks.

The most serious complication of pemphigus itself is loss of the skin's ability to protect the body from bacterial invasion, resulting in widespread skin or systemic infection. However, pemphigus is a chronic condition that requires ongoing medication therapy. For many people who have pemphigus vulgaris, the more common and more severe form, the most significant complications arise from the long-term use of the medications necessary to control outbreaks. These medications all have serious side effects and adverse consequences for other body structures and functions. Pemphigus that appears as an adverse DRUG reaction typically ends when the person stops taking the medication. Paraneoplastic pemphigus improves with treatment for the underlying cancer, though may cause life-threatening pulmonary complications when it affects the airways.

Risk Factors and Preventive Measures

Because doctors do not know the mechanisms that set pemphigus in motion, there are no identified risk factors. The condition tends to first manifest in people who are age 40 or older, though can occur at any age. Researchers suspect GENE mutations underlie pemphigus as they do other AUTOIMMUNE DISORDERS, though have not yet been able to identify them. Early diagnosis and aggressive treatment are key to mitigating symptoms and outbreaks, improving QUALITY OF LIFE as well as helping preserve other structures and functions. People who have milder forms of pemphigus may go extended periods without symptoms.

See also ANTIBODY; BLISTER; BULLA; BULLOUS PEMPHIGOID; KERATINOCYTE; LESION; MUTATION.

petechiae Smooth, reddened, pinpoint lesions that result from microscopic bleeding under the surface of the SKIN. Petechiae most commonly appear on the lower legs though can appear anywhere on the body. The presence of petechiae is a symptom that signals an underlying health condition that causes a low platelet count such as THROMBOCYTOPENIA, LEUKEMIA, MONONUCLEOSIS, or SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). Platelets are the body's first-line response in the COAGULATION process, clumping together (aggregating) to slow bleeding. Antiplatelet therapy such as ASPIRIN THERAPY, often prescribed for people at risk for HEART ATTACK or STROKE, intentionally blocks the actions of platelets and may also result in petechiae. The appearance of petechiae, which often is sudden, requires prompt evaluation from a doctor.

See also ECCHYMOSIS; LESION; MONONUCLEOSIS, INFECTIOUS; PLATELET; PURPURA.

photosensitivity A heightened reaction to sunlight or other ultraviolet light that results in a RASH or SUNBURN at much lower or shorter exposure than would ordinarily cause sunburn. Photosensitivity may develop as a reaction to a medication, such as the antibiotic medication tetracycline or the herbal antidepressant remedy ST. JOHN'S WORT (hypericum), or as a symptom of an underlying health condition such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) or ALBINISM. Photosensitivity may manifest as a red, splotchy rash on areas of SKIN exposed to the sun or as a full-fledged sunburn. Rarely, an individual may have an allergic reaction to ultraviolet light that causes the fairly immediate eruption of URTICARIA (hives) with sun exposure.

The dermatologist can diagnose photosensitivity based on its presentation and a history of recent sun exposure. Treatment may include topical or oral ANTIHISTAMINE MEDICATIONS if the rash itches (although topical antihistamines can themselves increase sun sensitivity). Topical CORTICOSTEROID MEDICATIONS often help reduce INFLAMMATION from widespread sunburn. However, the most effective treatment for photosensitivity is preven-

tion. Dermatologists recommend people who are photosensitive:

- wear clothing that covers the arms, legs, head, face, and neck when going outdoors, even when the day is cloudy
- liberally apply sunscreen at least 30 minutes before going outdoors (many dermatologists recommend applying sunscreen after getting out of the shower in the morning so the skin can absorb it) and frequently while outdoors
- avoid exposure during the sun's most intense periods, typically between 10 a.m. and 4 p.m. in most regions of the United States

See also ANTIBIOTIC MEDICATIONS; PHOTOPHOBIA; PORPHYRIA.

phototherapy Treatment with ultraviolet light, which suppresses the action of immune cells in the SKIN (T-CELLS). Ultraviolet light also slows the growth rate of keratinocytes, the cells that make up much of the dermis and nearly all of the epidermis, helping reduce symptoms such as plaque formation and scaling. Phototherapy is effective for numerous chronic dermatologic conditions, notably PSORIASIS, VITILIGO, and atopic DERMATITIS. Many people require therapeutic phototherapy to bring symptoms under control, with ongoing maintenance treatments to help prevent recurrent outbreaks or to continue subduing the IMMUNE RESPONSE. With appropriate protection to prevent ultraviolet damage to the eyes and skin, phototherapy has few short-term side effects. Questions remain, however, about long-term consequences such as the same problems that accompany extended sun exposure (notably SKIN CANCER). Dermatologists use three types of phototherapy: ultraviolet B (UVB) phototherapy, psoralen plus ultraviolet A (PUVA) phototherapy, and excimer laser phototherapy.

UVB phototherapy UVB lightwaves are less intense than ultraviolet A (UVA) lightwaves, achieving a therapeutic benefit with low risk of sunburn and other complications. UVB phototherapy was the first therapeutic application of ultraviolet light and remains the most common one in use today. Dermatologists use two forms of UVB phototherapy: broadband, the conventional UVB phototherapy, and narrowband, which employs a narrower width of ultraviolet light. Narrowband UVB phototherapy is often more effective for treating psoriasis, though has a higher risk of sunburn than broadband UVB phototherapy. For UVB phototherapy treatments, the person stands inside a small room called a light box with the areas of skin exposed that are to receive treatment. Other skin surfaces remain clothed or covered, though treatment may be appropriate for nearly the entire body.

PUVA phototherapy PUVA lightwaves provides a stronger, more focused therapeutic effect. UVA lightwaves are more intense than UVB lightwaves. Psoralen is a photosensitive substance taken orally as a pill or applied as a lotion to lesions and desired skin surfaces. Short exposures to UVA lightwaves activate the psoralen, which intensifies the effect. This combination reduces the risk for complications such as sunburn during treatment. However, the skin remains photosensitive for up to 36 hours after treatment, requiring the person to avoid all sun exposure for 12 to 36 hours following a PUVA phototherapy session. The individual must also wear sunglasses after taking oral psoralen because the psoralen tends to accumulate in the retinal tissues of the eyes. Some people have an ADVERSE REACTION to psoralen including NAUSEA, vomiting, itching (PRURITUS), and heightened sensitivity to sun exposure even after PUVA phototherapy ends.

Excimer laser phototherapy Another type of phototherapy is the excimer laser, which emits high-intensity UVB lightwaves that the dermatologist focuses on specific lesions or defined areas of the skin's surface. Such laser phototherapy allows targeted treatment and limits the risk for sunburn, though targeted lesions often acquire deeper pigmentation than the surrounding skin and may SCAR after HEALING. Often the hyperpigmentation fades over time. Dermatologists generally reserve excimer laser phototherapy for conditions that do not respond to other treatments.

See also KERATINOCYTE; LESION; NEONATAL JAUNDICE.

piercings Skin piercings for cosmetic purposes have become popular in the United States, especially among young people. Most people who have piercings experience minor complications at

some point. Wearing jewelry in the piercing, which is necessary to maintain the piercing, also establishes circumstances for HYPERSENSITIVITY REACTION and INFECTION. Long-term complications of piercings can include deformity of the tissues at the piercing site and the risk for systemic infection such as HEPATITIS.

Hypersensitivity Response

Contact DERMATITIS, often as a hypersensitivity reaction to the nickel in stainless steel, is the most common dermatologic complication of piercings. In contact dermatitis, the skin at the piercing location becomes red (erythema) and inflamed. It may itch or hurt. The piercing may swell, causing the tissue to close around the jewelry. Removing the jewelry and cleansing the site with an antiseptic solution made for this purpose helps soothe the irritated tissues and reduce INFLAMMATION.

Infection

Infection is a common problem that may develop as a complication of contact dermatitis, as a result of contaminated piercing needles and devices, or as a consequence of improper cleansing after piercing. Contamination is a significant risk with self-piercing. Early detection and treatment is important to prevent the infection from invading deeper tissues. EAR CARTILAGE piercings are particularly vulnerable to infection as well as resistant to treatment for infection, as the BLOOD supply to the area is sparse. Navel and genital piercings also are vulnerable to infection as a result of irritation from clothing and moisture.

Piercing jewelry made of plastic, wood, BONE, and other permeable materials can harbor BACTERIA. Minor infections generally improve with topical ANTIBIOTIC MEDICATIONS. More extensive infections require a doctor's evaluation and often require more involved treatment such as oral antibiotic medications and antiseptic cleansing of the piercing site.

Systemic infection such as hepatitis, and less commonly HIV/AIDS, is a significant risk when reusing or sharing piercing jewelry and needles. The hepatitis VIRUS can live outside the human body for extended periods of time. Piercings in and around the MOUTH carry the risk for bacterial infection that can involve the HEART valves because the mouth has a rich blood supply as well as an abundance of bacteria.

Deformity

Small piercings (16 gauge and smaller) will heal closed without scarring when the person no longer wears jewelry in the piercing to keep it open. Larger piercings (12 gauge and larger) may not heal closed, or may close with puckering of the tissue. Large-gauge piercings may stretch the tissues, such as the earlobes or lips, causing permanent enlargement. Infections, particularly of the ear cartilage, can destroy tissue, requiring PLASTIC SURGERY to restore the appearance and sometimes the function of the tissue. Piercings of the PENIS can damage or destroy erectile tissue, nerves, or the URETHRA. Clitoral piercing can damage nerves and cause structural damage to the CLITORIS and surrounding labia, particularly as a consequence of infection.

Preventing Piercing Complications

Basic hygienic methods can prevent most piercing complications. These methods include

- having piercings done by reputable, experienced professionals who use only disposable needles and equipment
- daily cleansing of piercing sites, such as washing with gentle soap and water during regular showering or bathing, or using a commercially available antiseptic cleansing solution for piercing sites
- frequently changing and cleaning piercing jewelry
- not sharing piercing jewelry
- wearing piercing jewelry made of impermeable materials such as metals

See also TATTOOS; VALVULAR HEART DISEASE.

pilonidal disease A chronic condition in which HAIR-filled cysts form at the base of the spine. The cysts typically originate when the SKIN closes to form saclike structures with hair trapped inside. The sac fills with fluid, cells, and other debris. Often there are indentations or pits over the tops of the cysts, and sometimes the hair within the

cyst protrudes out. Pilonidal cysts often remain symptomless, though many become apparent because they are subject to persistent irritation from clothing, movement, and pressure. Extended sitting, clothes that fit tightly across the buttocks, and activities such as bicycling often create awareness of pilonidal cysts.

The key symptoms of pilonidal disease are PAIN, swelling, erythema (redness), and drainage (pus) over the sacrum (tailbone). Often a FEVER accompanies these symptoms, and the person is unable to sit or walk without great discomfort. The doctor often can diagnose pilonidal disease based on the appearance of the cysts and the history of the symptoms. The doctor typically lances (cuts open with a sterile instrument) the cysts to allow them to drain. Large, purulent, or recurrent cysts may require surgery to remove them.

Pilonidal disease tends to be recurrent and persistent, often continuing throughout life. Surgically removed cysts seldom return, though new cysts frequently form in the same proximity. Keeping the area clean and wearing loose-fitting clothing can help prevent pilonidal cysts from becoming irritated. Frequent position changes when sitting and sitz baths (sitting in warm water) help reduce discomfort when cysts are present.

See also ABSCESS; ANAL FISSURE.

pityriasis rosea A common SKIN RASH in which an outbreak of lesions occurs and resolves over a period of 3 to 12 weeks, generally without treatment or complications. The lesions are characteristically oval with distinct borders and may be smooth (macules), raised (papules), or scaly (plaques). Often the lesions itch and sometimes they cause the skin to be hypersensitive to touch. Doctors believe a VIRUS causes pityriasis rosea.

Symptoms and Diagnostic Path

The primary symptom of pityriasis rosea is an itchy (pruritic) rash that appears on the back, chest, arms, and legs. There is usually an initial outbreak, called a herald LESION, with subsequent eruptions of lesions in other locations. Often the dermatologist will biopsy a lesion to confirm the diagnosis, as well as conduct BLOOD tests to rule out secondary SYPHILIS, which has a rash very similar to that of pityriasis rosea.

Pityriasis rosea is very similar in appearance to the rash that occurs with secondary SYPHILIS. As untreated syphilis has serious health consequences, the diagnostic path should include a blood test to rule out syphilis.

Treatment Options and Outlook

Treatment aims to relieve symptoms. Cool baths and skin moisturizers often are enough to relieve mild pityriasis rosea. Topical and oral ANTIHISTAMINE MEDICATIONS, and sometimes mild CORTICOSTEROID MEDICATIONS, are necessary to control itching. The lesions clear up on their own after about 8 weeks, though in some people the rash and itching may persist for up to 12 weeks.

Risk Factors and Preventive Measures

Doctors do not know what causes pityriasis though strongly suspect a virus. Outbreaks tend to occur among people who are in close proximity, commonly during the winter months. Complications are very uncommon though scratching can open the lesions and allow secondary infection to develop. Pityriasis rosea is a self-limiting condition so recovery is without residual effects.

See also MACULE; PAPULE; PLAQUE, SKIN; PRURITUS; PSORIASIS; TINEA INFECTIONS.

plaque, skin Raised, hardened, scaly lesions that form on the SKIN. Plaques characterize numerous dermatologic conditions. They may itch, hurt, or flake and may occur in small clusters or cover large areas of skin. Treatment for skin plaques targets the underlying conditions and includes measures to moisturize or soften the skin to help reduce the plaques. Topical CORTICOSTEROID MEDICATIONS or injections of corticosteroids into large plaques may help reduce them more quickly.

See also DERMATITIS; LESION; MACULE; NODULE; PAPULE; PSORIASIS; SCALE.

pressure sore See DECUBITUS ULCER.

prurigo A chronic condition in which lesions, typically papules or nodules, that itch intensely erupt on the SKIN. The lesions may occur anywhere on the body, though typically form in loca-

tions that allow scratching. Because the cause of prurigo, also called prurigo nodularis, remains unknown, dermatologists do not know whether the lesions develop in response to scratching or whether the itching of the lesions establishes the need to scratch. Whichever is the case, one perpetuates the other. The lesions eventually develop coarse, scaly surfaces. The intense itching drives many people to scratch the lesions until they bleed, which causes scabs to develop. Lesions that heal often leave white scars. An outbreak of lesions may extend over months or even years.

Prurigo is sometimes associated with LIVER disease, KIDNEY disease, HIV/AIDS, atopic DERMATITIS, GENERALIZED ANXIETY DISORDER (GAD), and also DEPRESSION. Most people who develop prurigo are middle-age or older, though occasionally the condition occurs in young people. The diagnostic pathway may include biopsy to rule out other causes for the lesions. Treatment generally incorporates topical CORTICOSTEROID MEDICATIONS and topical or oral ANTIHISTAMINE MEDICATIONS to subdue the itching. The dermatologist may choose to inject large or recurrent lesions with a corticosteroid medication. Some people who have prurigo benefit from psoralen plus ultraviolet A (PUVA) PHOTOTHERAPY or cryotherapy (freezing), which destroys the lesions and allows the skin to heal.

See also LESION; LICHEN SIMPLEX CHRONICUS; NODULE; PAPULE; PRURITUS; SCAR.

pruritus The clinical term for itching, especially itching that engenders the uncontrollable urge to scratch. Pruritus is a symptom of innumerable health conditions and may be localized (confined to a specific area or to lesions) or generalized (widespread, involving much of the SKIN's surface). The skin may appear reddened (erythema), swollen (edema) or otherwise irritated, or may show no reason for the itching.

The physiologic mechanism of itching is similar to, though distinctive from, that of PAIN. The NERVE cells, called nociceptors, that send itch signals to the BRAIN are scattered throughout the epidermis and upper layer of the dermis. Irritants that contact the epidermal and dermal layers of skin can arouse the nociceptors, coming from the external surface of the skin (such as from lesions that form on the skin) or from within (such as the accumulation of BILIRUBIN, which accounts for the itching that accompanies JAUNDICE). HISTAMINE, which the IMMUNE SYSTEM releases during a HYPERSENSITIVITY REACTION (allergy or ASTHMA), is among the internal stimuli that activate these nociceptors.

The response of scratching is a REFLEX that the autonomic NERVOUS SYSTEM generates in response to itch signals. Researchers theorize that scratching activates a mild pain response that overrides the itch response. Pain and itch appear to use many of the same nociceptors, and pain seems to be the more dominant stimulus. However, many factors contribute to the experience of itching as

HEALTH CONDITIONS ASSOCIATED WITH PRURITUS

adverse DRUG reaction	ANEMIA	BULLOUS PEMPHIGOID
CANDIDIASIS	CHICKENPOX	CHLAMYDIA
CIRRHOSIS	CONJUNCTIVITIS	DERMATITIS
DIABETES	dry SKIN	FOLLICULITIS
GENITAL HERPES	HEPATITIS	HERPES SIMPLEX
HYPERTHROIDISM	ICHTHYOSIS	IMPETIGO
JAUNDICE	LEUKEMIA	LICHEN PLANUS
LICHEN SIMPLEX CHRONICUS	LYMPHOMA	MEASLES
MILIARIA	parasitic infections	PEDICULOSIS
PEMPHIGUS	PILONIDAL DISEASE	PITYRIASIS
POLYCYTHEMIA VERA	PRIMARY BILIARY CIRRHOSIS	PRIMARY SCLEROSING CHOLANGITIS
PRURIGO	PSORIASIS	RENAL FAILURE
RUBELLA	SCABIES	TINEA INFECTIONS
URTICARIA	VAGINITIS	VULVODYNIA

well as to its relief. Scratching is also a conscious action, and can itself be an irritant that causes itching. Dermatologic conditions in which the itch/scratch relationship becomes circular include LICHEN SIMPLEX CHRONICUS and PRURIGO.

Pruritus is often an early indication of systemic health conditions such as jaundice or kidney dysfunction, and is a hallmark symptom of dermatologic conditions such as PSORIASIS and DERMATITIS. The diagnostic path depends on the complex of symptoms. Treatment may include topical or systemic ANTIHISTAMINE MEDICATIONS or CORTICOSTEROID MEDICATIONS and other therapies to resolve the underlying condition. It is important to resist the urge to scratch, as scratching further irritates the skin and may open the pathway for INFECTION.

See also ALLERGY TESTING; AUTOIMMUNE DISORDERS; LESION; RASH.

pseudofolliculitis barbae A condition in which large numbers of the hairs in the beard region on a man's face grow inward after shaving, causing irritation and INFLAMMATION. Pseudofolliculitis barbae, sometimes called razor RASH or razor bumps, occurs most frequently in men whose facial HAIR is tightly curled, and is particularly common among African American men. The process of shaving pulls the hairs before cutting them, allowing the cut tips to retreat within the hair follicle. When the facial hair is tightly curled the shaved tips of the hairs, which are pointed and sharp, turn into the sides of the follicle. As they grow they puncture the follicle rather than growing out of the follicle's opening, creating blocked follicles. The entire beard area often becomes involved, causing considerable discomfort and difficulty shaving.

The dermatologist can usually diagnose pseudofolliculitis barbae on the basis of its appearance, though may choose to scrape several of the inflamed papules (bumps) to rule out INFECTION. Shaving with an electric razor, which does not pull and cut the hair as much as a blade razor, may reduce symptoms for some men, though many men experience irritation and inflammation regardless of shaving method. When that is the case, the optimal solution is to stop shaving. Topical preparations such as benzoyl peroxide lotion or tretinoin cream are also sometimes helpful, though may themselves cause SKIN irritation.

See also FOLLICULITIS; INGROWN HAIR; PAPULE; TINEA INFECTIONS.

psoriasis A common, chronic SKIN condition in which the dermis produces keratinocytes at an accelerated rate. This causes immature keratinocytes, which are still soft, to reach the epidermis (the outer layer of the skin). The excess keratinocytes form lesions, typically scaly plaques, that itch (PRURITUS) or hurt. The accelerated turnover of keratinocytes creates an IMMUNE RESPONSE in the skin that dermatologists refer to as T-CELL activation. The immune response produces INFLAMMATION, the body's attempt to heal the plaques. But like the other components of psoriasis, the T-cell response is out of control and results in exacerbating, rather than relieving, the lesions.

Dermatologists believe GENE mutations establish a predisposition for the accelerations that characterize psoriasis. External or environmental circumstances such as injury, INFECTION, and stress then trigger the dysfunctions in the skin that result in the psoriasis. Psoriasis appears to run in families, suggesting that the mutated genes are inherited. Researchers continue to explore the genetic foundations of psoriasis. Once psoriasis manifests, it remains in a lifelong pattern of outbreak and REMISSION.

Generally, dermatologists classify five types of psoriasis. Psoriasis in any of these types can also cause inflammation of the joints, a form of arthritis called psoriasic arthritis. Dermatologists may also refer to psoriasis according to the parts of the body affected, such as palmar-plantar which affects the palms of the hands and soles of the feet. About 7 million Americans have psoriasis.

Erythrodermic psoriasis In erythrodermic psoriasis, widespread areas of the skin become red and scaly, and often swollen. This is the least common but most severe type of psoriasis. It can develop from any of the other types of psoriasis.

Flexural psoriasis Also called inverse psoriasis, flexural psoriasis forms smooth though itchy lesions in areas such as the axillae (underarms), creases of the leg in the groin, under the breasts, and other skinfold areas. Irritation from rubbing and sweating exacerbates the lesions.

Guttate psoriasis In guttate psoriasis, the second-most common type of psoriasis, the lesions

are small and look as though they were dropped onto the skin. The lesions have raised edges with centers that are somewhat depressed and appear crumpled. Guttate psoriasis is most common on the trunk, arms, legs, and scalp. The lesions itch, and may crack and then crust over before HEALING. Upper respiratory infections such as COLDS or PHARYNGITIS (notably STREP THROAT) often trigger outbreaks of guttate psoriasis.

PSORIASIS AND BLOOD DONATION

Some oral medications for psoriasis stay in the BLOOD for an extended time and have the potential to cause serious BIRTH DEFECTS. Blood banks defer people who take or who have taken these medications from donating blood for periods of time, depending on the medication. People who have taken etretinate at any time, which is no longer available, are permanently deferred because it remains in the blood indefinitely.

Plaque psoriasis The most common form of psoriasis, plaque psoriasis features erythematous (reddened) plaques that typically develop on the knees, elbows, scalp, and trunk. The plaques itch and sometimes hurt and often crack, bleed, and crust. Plaque psoriasis also can affect the fingernails and toenails, causing pitting, deformation, discoloration, and separation from the nail bed. Emotional and physical stress (such as illness or injury) may initiate outbreaks of plaque psoriasis. Some people have few outbreaks and other people have lesions nearly continuously.

Pustular psoriasis The lesions in pustular psoriasis look infected but simply contain fluid mixed with white blood cells, dead skin cells, and other matter that has the appearance of pus. Adverse DRUG reactions and topical irritants often trigger pustular psoriasis.

Symptoms and Diagnostic Path

The dermatologist diagnoses psoriasis primarily on the basis of its symptoms and history, and may choose to biopsy representative lesions to confirm. In its early stages, psoriasis may be difficult to distinguish from DERMATITIS and other skin disorders. The diagnosis becomes more conclusive when other family members have psoriasis.

Treatment Options and Outlook

The extent to which medical treatments can mitigate the symptoms of psoriasis depends on the type and severity of the psoriasis. Unfortunately, psoriasis responds unpredictably to treatment methods, with great individual variation. As well, the lesions may become resistant to specific treatments or medications over time, requiring a shift in therapeutic approach. This results in a trial-and-error approach that often frustrates those who have psoriasis. Dermatologists generally follow a sequential approach of progressively more intense therapy. Many people with moderate to severe psoriasis use a combination of therapies to help control their symptoms. ANTIBIOTIC MEDICATIONS may be necessary to treat secondary infections that affect psoriasis lesions.

Risk Factors and Preventive Measures

Because psoriasis has genetic predisposition, it is not possible to prevent its development. Once pso-

PSORIASIS SYMPTOMS

Type of Psoriasis	Characteristic Symptoms
erythrodermic	extensive scaly plaques; erythema (redness); INFLAMMATION; intense PRURITUS (itching)
	widespread SKIN involvement
flexural (inverse)	smooth, erythematous lesions
	skinfold areas, underarms, groin; pruritus with irritation such as sweating or rubbing
guttate	small, droplike lesions; cracks and crusting; mild to moderate pruritus
	trunk, arms, legs, scalp
plaque	erythematous, scaly lesions; cracks, bleeding, crusting; mild to moderate pruritus
	knees, elbows, scalp, trunk, fingernails, toenails
pustular	lesions that appear to contain pus; crusting while HEALING; mild to moderate pruritus
	trunk, arms, legs

TREATMENTS FOR PSORIASIS

Topical Medications		
alclomestasone	amcinonide	anthralin
betamethasone	calcipotriene	clobetasol
coal tar	desonide	desoximetasone
diflorasone	flumethasone	fluocinonide
flurandrenolide	halcinonide	halobetasol
hydrocortisone	methlprednisolone	mometasone
prednisolone	salicylic acid	triamconolone
Phototherapy		
PUVA phototherapy	excimer laser	ultraviolet B (UVB) phototherapy
Systemic Medications		
acitretin	alefacept	cyclosporine
efalizumab	etanercept	hydroxyurea
infliximab	methotrexate	mycophenolate mofetil
6-thioguanine	sulfasalazine	tretinoin

riasis manifests, it is important to receive prompt and appropriate medical treatment as well as identify and avoid triggers. Limited sun exposure, with precautions to prevent SUNBURN, may mitigate attacks and help the skin remain healthy.

See also BLOOD DONATION; BULLOUS PEMPHIGOID; JOINT; KERATINOCYTE; LESION; NAILS; PEMPHIGUS; STRESS AND STRESS MANAGEMENT.

purpura Smooth, moderately sized lesions, typically dark red to reddish purple, that result from bleeding under the surface of the SKIN. Purpura often look like small bruises and may occur anywhere on the body, including mucous membranes. The presence of purpura signals an underlying health condition resulting either from PLATELET deficiency, which delays COAGULATION (the clotting process), or bleeding due to systemic INFLAMMATION or INFECTION. As some of these underlying conditions are serious and potentially life-threatening, the appearance of purpura (except senile purpura and actinic purpura, which are common in aging skin) requires immediate medical evaluation. The doctor can distinguish purpura from other discolorations by applying gentle pressure to them. Purpura remain discolored, while other kinds of lesions often blanch (turn lighter).

CONDITIONS ASSOCIATED WITH PURPURA

adverse DRUG reaction	aging
ANAPHYLAXIS	congenital
congenital RUBELLA syndrome	CYTOMEGALOVIRUS (CMV)
immune thrombocytopenic purpura (ITP)	meningococcal SEPTICEMIA
ROCKY MOUNTAIN SPOTTED FEVER	thrombotic thrombocytopenic purpura (TTP)
VASCULITIS	

See also ECCHYMOSIS; LESION; PETECHIAE.

pustule A blisterlike formation that contains a pus, thick fluid of white blood cells, cellular debris, and sometimes BACTERIA. Pustules tend to hurt and sometimes itch. They commonly develop in numerous dermatologic conditions ranging from ACNE to FOLLICULITIS to PSORIASIS. Often pustules resolve without medical intervention, going away when the underlying condition causing them is under control. Warm, moist compresses or soaking and sometimes medications to reduce INFLAMMATION or fight INFECTION can speed HEALING. Topical or oral ANTIBIOTIC MEDICATIONS may be necessary when there is infection.

See also MACULE; NODULE; PAPULE.

PUVA therapy See PHOTOTHERAPY.

R

rash A general term for a broad range of SKIN eruptions. A rash is a symptom rather than itself a health condition and may accompany numerous dermatologic or systemic conditions. Viral and bacterial infections, immune and autoimmune responses, toxic contacts, systemic illnesses, chronic health conditions, and PARASITIC INFESTATIONS often cause rashes. Many rashes are so generalized that they are difficult to diagnose in the absence of other symptoms. Some rashes are so distinctive that their diagnosis requires no further symptoms. Nearly all rashes go away when the underlying health condition is resolved. Treatment for the rash may consist of approaches to mitigate symptoms, typically itching, and may include topical and oral ANTIHISTAMINE MEDICATIONS.

HEALTH CONDITIONS ASSOCIATED WITH RASH

adverse DRUG reaction	CHICKENPOX	DERMATITIS
HYPERSENSITIVITY REACTION	DIAPER RASH	FOOD ALLERGIES
rheumatic FEVER	LYME DISEASE	MEASLES
RUBELLA	MILIARIA	parasitic infestation
	RHEUMATOID ARTHRITIS	
	SCARLET FEVER	STREP THROAT

See also BACTERIA; IMMUNE RESPONSE; INFECTION; PRURITUS; PSORIASIS; VIRUS.

rhytidoplasty The clinical term for facelift, an OPERATION to smooth and tighten the SKIN on the face. Rhytidoplasty, also called rhytidectomy, is a cosmetic surgery appropriate for treating moderate to significant WRINKLES and sags on the face. There are numerous variations of rhytidoplasty that target only certain regions of the face or the whole face. Rhytidoplasty is generally an outpatient surgery (AMBULATORY SURGERY) with the person going home the same day. The operation generally takes three to six hours, though can take longer for a complex, total rhytidoplasty. Occasionally the surgeon may prefer to keep the person overnight in the hospital.

Before the operation the surgeon carefully marks the incision lines on the face with a surgical marking pen or permanent marker. Rhytidoplasty involves separating the skin from the underlying tissues, trimming away excess fat as well as skin, and reattaching the skin so it is tighter across the supporting tissues. Depending on the type of operation, the surgeon may also bolster the supporting tissues with suspension sutures to help them "lift" the face.

Swelling, discoloration, and PAIN are common following surgery, though ANALGESIC MEDICATIONS (pain relievers) can mitigate the pain. Many people experience pulling and stretching sensations during HEALING. Skin closures, usually sutures or staples, remain for 7 to 10 days. Bruising and swelling may remain for several weeks, as does numbness of the skin. Full recovery takes several months.

The risks of rhytidoplasty include excessive bleeding during as well as after surgery, INFECTION, permanent loss of sensation or NERVE damage, excessive scarring, separation of the tissues, and tissue death (NECROSIS). It is important to have realistic expectations around what the surgery can and cannot achieve and to understand the range of variation that is possible with regard to the final outcome. Though many people are satisfied with their appearance when healing is complete, there is an element of unpredictability as to the final result. Rhytidoplasty does not prevent further changes, such as those resulting from the natural aging process, from occurring. People who wish to maintain a specific appearance through cosmetic

surgery are likely to require multiple procedures over time. It is important to discuss these factors with the plastic surgeon.

See also AGING, INTEGUMENTARY CHANGES THAT OCCUR WITH; BLEPHAROPLASTY; RHINOPLASTY; SURGERY BENEFIT AND RISK ASSESSMENT.

ringworm See TINEA INFECTIONS.

rosacea An inflammatory condition that produces acnelike outbreaks and erythema (redness) on the face. Rosacea, sometimes incorrectly called adult ACNE, occurs primarily in people over age 40 and becomes more common with advancing age. Dermatologists do not know what causes rosacea, though believe it is an interaction between genetic and environmental factors. About 14 million Americans have rosacea. Though more women than men have rosacea, men tend to have more severe symptoms.

Symptoms and Diagnostic Path

The symptoms of rosacea are mild and general at first, often starting with increasingly frequent blushing. Dermatologists believe this early stage of rosacea may persist for years, though not many people seek medical care for it alone. Eventually the condition progresses to outbreaks of pimplelike pustules and other lesions that appear to be acne but resist conventional acne treatments. Most people seek a doctor's evaluation at this stage.

The typical symptoms that bring people to the dermatologist include

- extended flushing of the face and neck that may persist for hours after onset
- papules that erupt in clusters across the cheeks, on the chin and forehead, around the base of the NOSE, and sometimes around the eyelids
- itching and burning of the face, particularly in areas where papules have erupted
- patches of dry flaky skin when the papules retreat
- TELANGIECTASIS (fine BLOOD vessels that appear as red lines beneath the surface of the skin)
- CONJUNCTIVITIS and itchy, dry eyes
- rhinophyma (enlarged and bulbous nose) in advanced or severe rosacea

The dermatologist generally can make the diagnosis on the basis of the appearance and history of the symptoms and the person's age. Other factors that support a rosacea diagnosis include a personal or family health history of AUTOIMMUNE DISORDERS or rosacea symptoms.

Treatment Options and Outlook

Effective treatment for rosacea varies widely; what works for some people may have no effect for others. Dermatologists generally offer a combination approach of topical products and oral ANTIBIOTIC MEDICATIONS that are effective in controlling skin conditions. Most people who have rosacea try a number of treatments to find those that are the most effective.

COMMON TREATMENTS FOR ROSACEA

Topical	
azelaic acid	benzoyl peroxide
clindamycin topical	erythromycin topical
glycolic acid	metronidazole
sulfacetamide	sulfuric solutions
Oral	
doxycycline	erythromycin
minocycline	tetracycline

Laser therapy becomes a treatment option for rhinophyma and can reduce the size and shape of the nose to normal. Laser therapy is also useful for controlling telangiectasis. Treatment for EYE symptoms may include ophthalmic moisturizing solutions and CORTICOSTEROID MEDICATIONS to reduce INFLAMMATION and irritation. As rosacea is a chronic condition with no known cure, treatment is ongoing.

Risk Factors and Preventive Measures

People who are fair-skinned, blond, and blue-eyed seem most likely to develop rosacea. Because dermatologists do not know the precise mechanisms of rosacea, there are no known preventive measures. Factors that can sometimes trigger outbreaks of rosacea, though do not cause rosacea, include

- spicy foods

- CAFFEINE and ALCOHOL
- heat and strenuous physical exercise
- unprotected sun exposure
- strong emotional reactions such as anger, fear, or embarrassment
- hot showers or baths, hot tubs, saunas
- hormones (MENSTRUATION, PREGNANCY, MENOPAUSE)

Actions such as avoiding circumstances that trigger rosacea outbreaks, using sunscreen with a high sun-protection factor (SPF) when outdoors, and maintaining diligent therapeutic approaches can keep rosacea in check for many people who have the condition.

See also DERMATITIS; HORMONE; LESION; PERSONAL HEALTH HISTORY; PHOTOSENSITIVITY; PUSTULE; SUN PROTECTION.

S

scabies A contagious parasitic infestation with the SKIN mite *Sarcoptes scabei* that typically causes intense itching (PRURITUS) and visible bites or irritation to the skin. The bites create small, reddened papules (bumps) and often a RASH on the surrounding skin that is the burrows the mites make to lay their eggs. The most common sites for scabies are skinfold areas such as in the groin, under the breasts and armpits, between the shoulders, behind the knees, at the creases in the elbows, and on the inner wrists. Itching typically becomes intense at night. Aggressive scratching can cause secondary bacterial infections of the skin to develop. Scabies spreads through close physical contact.

The doctor diagnoses scabies with skin scrapings of the papules or rash. Microscopic examination of the scrapings often reveals eggs or fecal matter from the mites. Applying a lotion that contains a pesticide such as permethrin, lindane, or crotamiton will kill the mites, though the itching may persist for a few days. All members of the household should receive treatment. It is also important to wash clothing, towels, and bed linens in very hot (130°F) water for at least 10 minutes as a precaution to kill any mites these items might be harboring, as mites can live outside the body for up to 36 hours. Reinfestation may occur with reexposure.

See also BACTERIA; INFECTION; PAPULE; PARASITES; PEDICULOSIS.

scale A SKIN LESION in which keratinocytes clump together instead of falling away from the skin, adhering to the skin. Keratinocytes separated from the epidermis are nearly translucent, often giving scales a silver or white cast. When enough scales accumulate, their weight causes them to finally drop from the skin, often as visible flakes such as characterize DANDRUFF.

See also DERMATITIS; ICHTYOSIS; KERATINOCYTE; PLAQUE, SKIN; PSORIASIS; SEBORRHEIC KERATOSIS.

scar A formation of fibrous tissue that remains at the site of a healed wound. Though a scar will not entirely match the surrounding tissue, most scars heal to be barely noticeable.

Some scars become overgrown. A hypertrophic scar is enlarged though does not extend beyond the original wound site. Over time, most hypertrophic scars retreat to become less noticeable. The dermatologist may reduce a hypertrophic scar by injecting it with an intralesional corticosteriod medication or with pulsed dye laser treatments. The success of such procedures depends on the location and nature of the hypertrophic scar.

KELOID scars occur when the scar formation process continues after the wound heals. The keloid continues to grow, becoming a spongy LESION that no longer has anything to do with wound HEALING. Keloids can become quite large. The dermatologist may remove keloids that are continually irritated, such as by clothing, or that are cosmetically undesirable. However, keloids tend to recur.

See also PLASTIC SURGERY.

sebaceous glands The small glands that produce sebum, a lipid-based, oily fluid that lubricates the surface of the SKIN. Sebum is mostly the metabolic waste that remains after fat cells break down. Most sebaceous glands empty into HAIR follicles, secreting sebum along the emerging hair shaft. Some sebaceous glands exist independent of hair follicles and secrete sebum directly to the skin's surface, such as those on the glans of the PENIS.

The palms of the hands and the soles of the feet are the only skin surfaces that do not have sebaceous glands.

The oily consistency of sebum gives the skin a highly water-resistant coating. The lubricating qualities of sebum keep the keratinocytes, the cells that make up the epidermis, supple and flexible. Without adequate lubrication the skin becomes dry and the keratinocytes scale and flake, presenting not only an undesirable cosmetic appearance but also compromising the skin's resistance against pathogenic (disease-causing) microorganisms. Sebum also helps regulate the skin's natural flora, the collective of BACTERIA, yeasts, and other microscopic organisms that inhabit the epidermis. These microorganisms draw nutrients from the lipids in the sebum.

For further discussion of the sebaceous glands within the context of integumentary structure and function, please see the overview section, "The Integumentary System."

See also ACNE; DANDRUFF; KERATINOCYTE; SWEAT GLANDS.

seborrheic keratosis A condition in which noncancerous (benign) growths arise on the SKIN. The lesions resemble warts though appear pasted on rather than attached to the skin. The lesions are most commonly brown or black, though may be yellow, gray, tan, or other colors. Seborrheic keratosis becomes increasingly common in people age 40 and older. Most people develop multiple lesions. The lesions cause no symptoms beyond their presence, unless frequent irritation causes them to itch, hurt, or bleed.

Seborrheic keratosis requires medical assessment only to ascertain that the lesions are not cancerous, which typically is apparent on the basis of their appearance and history. The doctor should biopsy any lesions that are questionable. There is no medical reason to remove the lesions once diagnosed, however, as they do not turn malignant. People sometimes want lesions removed that are cosmetically undesirable or in locations where they receive frequent irritation such as from clothing. Cryotherapy (freezing), curettage and electrodesiccation (scraping and burning), and shave excision (cutting out; requires no sutures) are the most common methods of removal. Though removed lesions do not recur, others may grow nearby.

See also ACROCHORDON; LESION; NEVUS; SKIN SELF-EXAMINATION; WART.

skin The body's largest organ, making up the body's covering and about 15 percent of the total body weight The skin's three layers—epidermis, dermis, and subcutaneous layer—help the body maintain its structure; protect against INFECTION; and regulate fluids, electrolytes, and temperature. Numerous health conditions, localized and systemic, can affect the skin and its functions.

The subcutaneous layer, innermost to the body, contains primarily adipose tissue more familiarly called body fat. The dermis, the middle layer, provides the structure of the skin. It contains connective tissue, the SEBACEOUS GLANDS, and an abundant supply of nerves and blood vessels. The dermis nourishes the epidermis above it and attaches to the subcutaneous layer beneath it, holding the skin in place. HAIR follicles and SWEAT GLANDS extend from the epidermis into the dermis and a bit into the subcutaneous layer.

The primary cells of the skin, melanocytes and keratinocytes, originate in the base, or basal, level of the epidermis. Keratinocytes migrate outward to form the upper epidermis, gradually flattening and hardening. The epidermis varies in thickness and other characteristics, accommodating the needs of different body surfaces. The epidermis of the palms of the hands and the soles of the feet is thick and tough, for example, while that of the eyelids is soft and only two or three cells in depth.

The skin is also the body's organ of tactile sensory perception, or touch. Millions of NERVE endings in the skin continually sense environmental factors such as pressure, temperature, moisture. Other specialized nerve cells, called nociceptors, perceive itching and PAIN. Sweat evaporation on the skin's surface is the body's primary cooling mechanism, as well as a secondary mechanism for electrolyte regulation and balance.

For further discussion of the skin within the context of integumentary structure and function, please see the overview section "The Integumentary System."

See also KERATINOCYTE; MELANOCYTE; NAILS; SEBACEOUS GLAND.

HEALTH CONDITIONS THAT MAY AFFECT THE SKIN

ACNE	ACROCHORDON	ACTINIC KERATOSIS
ALBINISM	BIRTHMARK	BLISTER
BULLA	BULLOUS PEMPHIGOID	CALLUS
CARBUNCLE	CELLULITIS	CORNS
CRADLE CAP	DECUBITUS ULCER	DERMATITIS
DISCOID LUPUS ERYTHEMATOSUS (DLE)	EPIDERMOLYSIS BULLOSA	ERYSIPELAS
ERYTHEMA MULTIFORME	ERYTHEMA NODOSUM	FOLLICULITIS
FROSTBITE	FURUNCLE	HYPERHIDROSIS
ICHTHYOSIS	IMPETIGO	KAPOSI'S SARCOMA
KELOID	LICHEN PLANUS	LICHEN SIMPLEX CHRONICUS
MILIARIA	NEVUS	PAPILLOMA
PEDICULOSIS	PEMPHIGUS	PILONIDAL DISEASE
PITYRIASIS	PRURIGO	PSORIASIS
ROSACEA	SCABIES	SEBORRHEIC KERATOSIS
SKIN CANCER	SUNBURN	TINEA
TOXIC EPIDERMAL NECROLYSIS	URTICARIA	VITILIGO
WART	WHITLOW	XANTHOMA

skin cancer Malignant growth that arises from the epidermis or dermis. There are many types of CANCER that occur in the SKIN. The three most common types of skin cancer are basal cell carcinoma, squamous cell carcinoma, and malignant melanoma. Skin cancer is the most widely diagnosed type of cancer in the United States, with about 1 million new cases each year. The vast majority of skin cancers—basal cell carcinoma and squamous cell carcinoma—are nearly 100 percent curable with early detection and treatment. Malignant melanoma, the least common form of skin cancer, is more dangerous because it tends to metastasize (spread) early in its development, though it also has a high cure rate when detected and treated before it metastasizes.

Cancer experts believe nearly all skin cancer results from sun damage to the cells of the skin. The ultraviolet lightwaves the sun emits cause subtle changes in the ways skin cells function. Over time these changes can result in aberrant growth, causing skin cells to form into cancerous lesions. People with fair skin are most vulnerable to this damage, as their skin produces less melanin. In addition to giving the skin its color, melanin protects the skin from the sun by absorbing the ultraviolet lightwaves that cause damage. A tan paradoxically results from and protects the skin against sun exposure, as sun exposure stimulates melanocytes to produce melanin.

The ultraviolet light used in tanning booths affects the SKIN in the same way as the ultraviolet lightwaves of the sun, and carries the same exposure risk for skin cancer.

The correlation between sun exposure and skin cancer also means that nearly all skin cancers are highly preventable. Cancer experts recommend diligent SUN PROTECTION measures beginning in early childhood in combination with regular skin examinations to detect suspicious growths or changes in existing lesions. Other types of cancer that can affect the skin, but are not primary skin cancers or related to sun exposure, include KAPOSI'S SARCOMA, primarily a manifestation of HIV/AIDS in the United States, and cutaneous T-cell LYMPHOMA.

Basal Cell Carcinoma

Basal cell carcinoma is a cancer of the keratinocytes that form the bottom, or base, of the epidermis, also called basal cells. Most basal cell carcinomas erupt around HAIR follicles, leading researchers to suspect they originate in the follicle

structure or the SEBACEOUS GLAND (sometimes collectively called the pilosebaceous unit). Basal cell carcinomas nearly always arise on sun-exposed skin surfaces, though may also occur on skin exposed to radiation such as for RADIATION THERAPY.

The characteristic symptoms of basal cell carcinoma are

- open sore that does not heal
- reddened or flaky patch that itches or hurts
- shiny, discolored NODULE (bump) that develops on the skin
- pinkish, craterlike structure with raised edges and tiny BLOOD vessels visible in the center
- yellowish, waxy area that resembles a scar though gradually enlarges and may itch

Though basal cell carcinomas rarely metastasize, they do spread within the epidermis and can cause considerable damage to the skin. Doctors diagnose about 800,000 Americans with basal cell carcinoma each year, making it the most common cancer of any type. A person who has one basal cell carcinoma is likely to develop others, though removed tumors seldom recur. Basal cell carcinoma is uncommon in dark-skinned people.

Squamous Cell Carcinoma

Squamous cell carcinoma is a cancer of the keratinocytes in the upper layer of the epidermis, formerly called squamous cells because of their squamous, or squashed, appearance. Nearly all squamous cell carcinoma evolves from ACTINIC KERATOSIS (though not all actinic keratosis lesions become cancer). Because of this, doctors consider actinic lesions precancerous and remove them to end their progression, effectively thwarting the cancer's development. Squamous cell carcinoma can but does not often metastasize. Sun damage causes most squamous cell carcinoma, though tumors can form in sites of continual irritation.

The characteristic symptoms of squamous cell carcinoma are

- crusted, raised growth resembling a WART that easily or frequently bleeds
- patch of red, flaky skin that oozes or bleeds
- sore that bleeds and crusts but does not go away
- ulceration on the lips that resembles a COLD SORE but does not heal

Though most commonly a cancer of the surface skin (particularly sun-exposed), squamous cell carcinoma also can develop in the mucous membranes. Untreated squamous cell carcinoma will eventually grow downward to penetrate the dermis and subcutaneous layer, and may spread to LYMPH structures that enable widespread metastasis. Doctors diagnose about 200,000 Americans with squamous cell carcinoma each year. Though squamous cell carcinoma is less common in dark-skinned than in light-skinned people, among skin cancers in dark-skinned people squamous cell carcinoma is the most common.

Malignant Melanoma

Malignant melanoma arises from melanocytes, the cells that produce melanin. Benign skin lesions such as nevi (moles) composed of melanocytes are often the staging sites for malignant melanoma. Malignant melanoma can develop and metastasize quickly. Diligent monitoring for changes in existing lesions such as moles is the most effective method for early detection and diagnosis. Doctors classify malignant melanoma by growth pattern (such as nodular, superficial, or spreading) or by depth of invasion, metastasis, and nodal involvement. Small, localized malignant melanomas are about 90 percent curable with early diagnosis and treatment. Widely metastasized malignant melanoma is usually fatal.

The characteristic symptoms of malignant melanoma are

- change in the size, symmetry, color, or texture of an existing NEVUS (mole)
- bleeding or oozing from an existing nevus
- a new nevus that emerges and grows rapidly, especially one that has asymmetrical shape, irregular borders, multiple colors, or exceeds one quarter inch in diameter (the ABCD criteria)

Doctors diagnose about 50,000 Americans with malignant melanoma each year, many of whom have moderate to advanced cancer by the time of diagnosis.

ABCD CRITERIA FOR MALIGNANT MELANOMA

A = asymmetry; halves do not match
B = borders; edges are irregular or vague
C = color; two or more colors are present
D = diameter; larger than one quarter inch

Symptoms and Diagnostic Path

Symptoms vary among the types of skin cancer, though generally any wound or sore that does not heal or mole that changes appearance is suspect. The diagnostic path typically includes biopsy of suspicious lesions. The dermatologist may remove very small lesions without biopsy, as doing so effectively removes any cancer that is present. Biopsy identifies the type of cancer present, which determines the appropriate course of treatment.

CHARACTERISTIC SKIN CANCER SYMPTOMS

Type of Skin Cancer	Characteristic Symptoms
basal cell carcinoma	sore that does not heal persistent red or flaky patch that itches shiny, discolored NODULE vascular crater yellowish, waxy, itchy plaque
squamous cell carcinoma	wartlike lesion that bleeds flaky patch that bleeds sore that repeatedly bleeds and crusts lip ulceration that does not heal
malignant melanoma	ABCD criteria: • asymmetrical appearance • irregular borders • multiple colors • diameter greater than one quarter inch

Treatment Options and Outlook

The preferred treatment for nearly all skin cancer is surgical removal, which may include various methods such as curettage and electrodesiccation (scraping and cauterization), excision (cutting out), and MOHS' MICROGRAPHIC SURGERY. Microscopic examination of the removed LESION confirms the diagnosis and type of cancer. Malignant melanoma requires extensive excision, with wide margins and possible removal of nearby LYMPH NODES, and may require follow-up CHEMOTHERAPY if the cancer has metastasized. Dermatologists may use cryotherapy (liquid nitrogen) to remove precancerous lesions, such as those of actinic keratosis, and very small lesions that appear suspicious. Other treatment options may include topical imiquimod (Aldara) cream and RADIATION THERAPY.

Risk Factors and Preventive Measures

The single-most important risk factor for skin cancer is excessive sun exposure. People born before the 1980s have the highest risk for skin cancers because they grew up before sunscreen products became available. Skin cancers tend to manifest several decades after the exposures that damaged the skin, making it important for people age 40 and older to have yearly skin examinations from a physician and to perform monthly SKIN SELF-EXAMINATION. People who have had skin cancers removed may need more frequent physician evaluation. The most effective preventive measures are those that safeguard the skin from sun damage. These measures include

- limit sun exposure during peak ultraviolet intensity (10 a.m. to 2 p.m. in most of the United States)
- wear protective clothing to cover the skin
- apply sunscreen liberally and frequently before and during sun exposure

See also CANCER RISK FACTORS; CANCER TREATMENT OPTIONS AND DECISIONS; KERATINOCYTE; MELANOCYTE.

skin replacement A procedure for restoring SKIN to areas of the body where there has been extensive damage and loss of skin. BURNS, major trauma, surgery, varicose ulcers, and decubitus ulcers are among the conditions that require skin replacement. Skin-replacement techniques may use skin grafts or synthetic skin products for temporary or permanent reconstruction.

Skin Grafts

There are three main sources for skin grafts:

- autograft, which harvests skin from one location on the person's body and transplants to another for permanent skin replacement

- allograft, which uses donor skin harvested from a cadaver to create temporary protection while the wound heals enough to accept a permanent graft
- xenograft, which uses specially prepared skin from an animal, usually a pig (porcine xenograft), to create temporary protection while the wound heals enough to accept a permanent graft

An autograft has the highest rate of success because it is the person's own tissue. A skin graft may be full thickness, which includes the complete epidermal and dermal layers, or split thickness, which includes the epidermal and upper dermal layer. A full-thickness graft generally produces a better cosmetic result though carries a higher risk of failure. A split-thickness graft generally adheres, or "takes," better though may heal somewhat irregularly.

Synthetic Skin

Synthetic skin uses materials crafted in the laboratory to create a substitute skin that may serve as a temporary covering or a matrix to support permanent new skin growth. Typically the matrix consists of two layers: one that the new cells grow into and that remains a permanent part of the skin and the other one, usually made of silicone or a similarly inert material, the surgeon removes when HEALING is well established. The new skin grows through the synthetic matrix, absorbing it into its structure.

Surgical Procedure

Skin replacement may be an outpatient or inpatient OPERATION, depending on the nature of the wound. If using an autograft, the surgeon first harvests the graft from the donor site. With an autograft or allograft, the surgeon typically uses a device called a mesher to put tiny holes evenly throughout the graft. This meshing allows the graft to stretch to cover a larger area. The holes also allow fluid to drain from the site, improving healing. After about 36 hours, the graft begins to develop new BLOOD vessels that tether it to the underlying tissue and provide a source of nourishment. Xenografts typically arrive already meshed and ready to place, needing only for the surgeon to trim them to the appropriate size. Synthetic grafts do not require meshing and are also ready to place. TISSUE EXPANSION is a method that allows the surgeon to literally stretch the growth pattern of existing skin to grow extra skin the surgeon can then harvest and place where needed. It takes several months to grow enough skin to use for a graft.

Risks and Complications

The main risk of skin replacement is graft failure, which can occur regardless of the graft source. Numerous factors contribute to graft success or failure. The graft may fail to develop an adequate blood supply or the match between the donor graft and the recipient site may be not quite right. The underlying tissue foundation may not be adequate to support new skin growth. Other potential complications include excessive bleeding during or after surgery and INFECTION.

Outlook and Lifestyle Modifications

Small grafts that heal without complications may require few lifestyle changes. Large wounds may require extended rehabilitation and significant lifestyle modifications. With more extensive skin replacement, there may be continued care needs. The overall outlook depends more on the reason for the skin replacement than the replacement itself. The recipient site remains more vulnerable than native skin to damage from sun exposure and trauma.

See also DECUBITUS ULCER; HAIR TRANSPLANTATION; SUN PROTECTION.

skin self-examination A method for early detection of suspicious and possibly cancerous lesions on the SKIN. Health experts recommend skin self-examination monthly for adults. Doing skin self-examination takes 5 to 10 minutes and requires privacy to fully undress, a full-length mirror, and a handheld mirror. Many people find it convenient to do a skin self-examination before or after bathing or showering. Use the mirrors to visualize and examine the entire skin surface including the bottoms of the feet and the genitals. A handheld hair dryer may help to examine the scalp. Look for skin blemishes and moles, and compare them to the ABCD SKIN CANCER screening characteristics

ABCD SKIN EXAMINATION

	Characteristic	Normal	Suspicious
A	asymmetry	matching halves (symmetrical)	unequal or nonmatching halves (asymmetrical)
B	border	smooth, even edges	ragged, notched, or otherwise uneven edges
C	color	single shade of brown	varied shades of brown; multiple colors
D	diameter	less than one quarter inch	larger than one quarter inch

for malignant melanoma. After doing several skin self-examinations, most people are familiar with their usual lesions and blemishes and can quickly identify any changes that have taken place since the previous self-exam. A dermatologist should evaluate any suspicious findings.

See also ACTINIC KERATOSIS; LESION; SEBORRHEIC KERATOSIS.

skin tag See ACROCHORDON.

staphylococcal scalded skin syndrome A potentially life-threatening bacterial INFECTION of the skin that most commonly affects infants and young children. *Staphylococcus aureus* is the infective agent. The infection is systemic, causing eruptions on the skin that give the appearance of scalding. A single LESION heralds the onset of the infection, with multiple lesions rapidly emerging. The lesions are scarlet red and quickly BLISTER. The blisters (bullae) are very fragile and peel away from the skin with touch. The lesions spread to be contiguous with one another, covering large portions of the body. The loss of skin exposes the body to other pathogens that can cause complicating infections and means the body cannot maintain proper thermal or fluid regulation. Prompt diagnosis and treatment with ANTIBIOTIC MEDICATIONS is essential. Most children fully recover with appropriate treatment. The infection is highly contagious. Diligent HAND WASHING is crucial for caregivers and family members.

See also BACTERIA; BULLA; PATHOGEN; TOXIC EPIDERMAL NECROLYSIS; TOXIC SHOCK SYNDROME.

Stevens-Johnson syndrome See TOXIC EPIDERMAL NECROLYSIS.

stretch marks Irregular, discolored streaks or lines in the SKIN. Stretch marks represent, as the name suggests, changes in the tissue structure and appearance that result from the skin stretching and separating from the underlying supportive tissues. Such stretching most commonly occurs with PREGNANCY, BREAST augmentation surgery, and weight gain and loss, and affects the abdomen, upper arms, thighs, and breasts. Early stretch marks appear pink; mature stretch marks are generally pale. In addition to the altered pigmentation, stretch marks may have a different texture than the surrounding skin. Stretch marks are cosmetic and do not affect health or reflect health conditions. Cosmetic treatments to minimize the appearance of stretch marks include laser therapy and topical products such as glycolic lotions and tretinoin cream.

See also PLASTIC SURGERY.

sunburn Damage to the epidermis and sometimes the dermis, the top and middle layers of the SKIN, as a consequence of extended, unprotected sun exposure. The sun emits several wavelengths of ultraviolet light. Those that reach the earth's surface are ultraviolet A (UVA) and ultraviolet B (UVB). Each affects the skin in different ways. UVA activates melanocytes, the cells that produce melanin (pigment) and may produce a thermal (heat) response that causes the skin to turn red. Though the skin may feel hot, this is not actually sunburn but rather a thermal (heat) response.

Sunburn is a delayed response to UVB exposure. UVB lightwaves do not activate the melanocytes but instead affect keratinocytes. When the epidermis (skin's outer layer) contains deeply pigmented keratinocytes, such as in a person who has dark skin or a tan from previous sun exposure, the pigment (melanin) absorbs the UVB and the keratinocytes escape damage. When the skin is light, melanin distribution is also light and there is little absorption of UVB.

The keratinocytes bear the brunt of the exposure, and about 8 to 12 hours later show the consequences. The damaged cells release toxins and other substances that draw increased BLOOD flow to the dermis. The additional blood flow causes the skin to become red (erythema). These toxins irritate the nerve endings in the epidermis and dermis, causing PAIN. Fluid may accumulate between the cells (edema), causing swelling. With more severe damage, fluid-filled blisters form on the skin. Discomfort peaks about 48 hours after exposure. At about this same time, the melanocytes have infused keratinocytes migrating from the dermis to the epidermis with melanin, giving them a darker pigment that will offer better protection than their predecessors had.

The most effective treatment for sunburn is a combination of moisturizing lotion or gel such as aloe vera to soothe the irritated skin and a nonsteroidal anti-inflammatory drug (NSAID) such as ibuprofen to relieve INFLAMMATION and pain. Most sunburn discomfort resolves in three to five days. Badly sunburned skin that has blistered is likely to peel at this point and requires gentle cleansing to minimize the risk for bacterial INFECTION until the new skin completely heals. Researchers now believe one significant sunburn is sufficient to lay the groundwork for skin cancer decades later. Repeated mild to moderate sunburns appear to have similar effect. Sunscreens and protective clothing worn during sun exposure can protect against sunburn.

See also BLISTER; BURNS; KERATINOCYTE; MELANOCYTE; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); SKIN CANCER; SKIN SELF-EXAMINATION; SUN PROTECTION.

sun protection Methods to safeguard the SKIN from SUNBURN and sun damage. Though the body requires a certain amount of sun exposure to produce certain vitamins (such as vitamin D) and help eliminate chemical wastes from the body, ultraviolet light is a potential hazard for the cells. Melanin production, which results in darkening the skin, is the body's primary method for protecting itself. The lighter a person's natural skin color, however, the less effective this method. Many health conditions that affect the skin, most notably SKIN CANCER, result from overexposure to the sun and in particular to ultraviolet B (UVB) light.

Protective Clothing

Clothing that covers or shades the skin surfaces is the most effective protection from sun exposure and can block more than 90 percent of the sun's ultraviolet light, though it is still possible to acquire a sunburn through clothing. Fabric with a tight weave is more effective than fabric with a loose weave. Many items currently manufactured specifically for outdoor activities now use yarns and weaving techniques that substantially block ultraviolet light. Manufacturers use ultraviolet-protection factor (UPF) ratings to designate the extent of the fabric's ability to prevent ultraviolet light penetration. The higher the UPF rating, the more effective the protection. Solid-weave, broad-brimmed hats help protect the scalp and shelter the ears, NOSE, and back of the neck. Technical gear for many outdoor sports, such as bicycling and kayaking, includes gloves that protect the hands from friction and pressure as well as sun exposure. Sunglasses that block UVA and UVB light are necessary to shelter the eyes.

A sunscreen product's SPF rating applies only to UVB blocking, so it is important to read the product label to determine what protection the product can provide.

Sunscreen

Sunscreens that chemically block ultraviolet light from penetrating the skin's surface became available in the 1980s. These chemicals work by absorbing the light so it does not reach the cells. Most sunscreens block UVB; some also block UVA. A sunscreen's sun-protection factor (SPF) rating, provides a general idea of how long the product can provide protection based on a time-related formula. In general, a fair-skinned person will get a sunburn after about 10 minutes of unprotected exposure to the sun. A sunscreen's SPF rating is a multiplier of that marker. A sunscreen with an SPF rating of 15, for example, theoretically permits 15 times as long in the sun before burning, or 150 minutes. A sunscreen with an SPF of 30 would allow 300 minutes. These are general guidelines, however, and dermatologists recommend applying more sunscreen about every two

hours during exposure (as well as SPF lip balms to protect the lips). Dermatologists recommend sunscreens that block both UVA and UVB lightwaves.

Because both sunscreen use and skin cancer are on the rise, some researchers have questioned whether sunscreens cause, rather than prevent, skin cancer. Though there are few clinical studies of such a correlation, so far there is no evidence to support this concern. Nor is there evidence to support claims that sunscreens promote estrogenic activity in the body, another concern that some people have raised. Health experts agree that proper application of sunscreen is the most effective defense to protect the skin from damage.

Time of Exposure

The sun's ultraviolet light is most intense from 10 a.m. to 2 p.m. in the United States. Health experts recommend staying out of the sun as much as possible during that period of time, especially during summer months. When this is not practical, dermatologists recommend combining protective clothing and sunscreen for maximum protection.

See also CANCER RISK FACTORS.

sweat glands Structures within the dermis layer of the SKIN that produce sweat as part of the body's temperature-regulation mechanisms. There are two kinds of sweat glands—eccrine and apocrine, both of which arise from the dermis.

Eccrine sweat glands are functional from shortly after birth and are present in all skin. An individual has between two and three million eccrine sweat glands that produce about 20 liters of sweat in 24 hours and can double or triple their production rate during strenuous exercise or heat conditions. Eccrine sweat glands open through pores directly onto the surface of the skin (pores), releasing sweat for rapid evaporation to cool the skin and lower body temperature.

Apocrine sweat glands are present only under the arms and in the pubic region, though are abundant in these regions. Although present from birth, they are nonfunctional until PUBERTY activates them. The apocrine sweat glands empty into HAIR follicles rather than directly onto the skin's surface. The sweat the apocrine glands produce contains lipids and proteins, which helps the sweat mix with the sebaceous fluids in the hair follicles to reach the skin's surface. BACTERIA on the surface of the skin consume the lipids and proteins, creating waste byproducts that produce the characteristic odor associated with sweating.

For further discussion of the sweat glands within the context of integumentary structure and function please see the overview section "The Integumentary System."

See also HEAT EXHAUSTION; HEAT STROKE; HYPERHIDROSIS; MILIARIA.

T–U

tattoos A form of body art in which decorative inks injected into the dermis permanently stain the SKIN. Though the needles are solid, they create puncture wounds that then fill with ink. The cells and intracellular spaces of the dermis absorb the ink. The health implications of tattoos are twofold: potential complications at the time of tattooing and the challenges of tattoo removal.

Commercial tattoo artists use mechanical needles that rapidly inject inks. The needles and the ink packets are sterile and for one-time use. Though inks are generally of natural origins, some people have adverse reactions to them that can cause swelling, INFLAMMATION, and scarring. Though many tattoo artists follow appropriate antiseptic procedures, many others do not. Most US states do not have regulations or procedures to establish health standards or confirm their practice.

The most common risk arising from improper skin and equipment cleansing is bacterial INFECTION of the tattooed site, which may require treatment with ANTIBIOTIC MEDICATIONS. A less common though far more serious infection risk is that of HEPATITIS and HIV/AIDS, both of which are bloodborne viral infections. Reusing needles and inks passes any VIRUS present to subsequent clients. Improperly cleaning the tattooing equipment also allows viruses to linger, with the potential of passing them on.

Tattoo removal is far less certain than tattooing. Most methods cause significant scarring. A form of laser therapy called Q-switched laser offers the least destructive means for removing tattoos. Lasers can destroy the structure of some inks without damaging the surrounding cells. The body's normal processes then remove the ink fragments as cellular debris. However, this process is most effective with black and blue inks, and least effective with yellow, red, and orange. Different wavelengths of laser are necessary for the various colors, so tattoo removal may involve several sessions. Seldom can the laser remove all color, though it often can remove enough color for the tattoo to appear only as a slight discoloration of the skin. It is possible for the pigment to darken in the skin surface surrounding the tattoo, in response to the laser. Scarring and infection also remain slight risks. Other methods of tattoo removal, such as DERMABRASION and excision, may more successfully remove the full tattoo though leave considerable scarring. With these methods, skin grafts are sometimes necessary.

See also BACTERIA; PIERCINGS; PLASTIC SURGERY; SCAR.

telangiectasis A weblike network of BLOOD vessels that becomes visible just below the surface of the SKIN, commonly called spider veins. Sometimes telangiectasis is present from birth or early childhood as a BIRTHMARK, though more commonly develops later in life as a manifestation of chronic sun exposure. Telangiectasis generally has no adverse health effects, though many people find the lesions cosmetically unacceptable. For telangiectasis on the face, dermatologists use laser therapy or fine cautery. For spider veins on the legs, the most common treatment is sclerotherapy in which the dermatologist injects the telangiectasis with a chemical that irritates the blood vessels, causing them to SCAR. Over time the discoloration fades. Laser therapy may be a therapeutic option for some telangiectasis lesions.

See also LESION; VARICOSE VEINS; VEIN.

tinea A common fungal INFECTION of the SKIN, involving the layers (including the hair and nails) that are cornified (composed of dead keratinocytes). Several species of fungi, known collectively as dermatophytes, cause tinea infection (also called dermatophytosis). People commonly refer to some forms of tinea as ringworm because the lesions have the appearance of worms ringed beneath the surface of the skin. Though descriptive this is a misnomer as tinea has nothing to do with worms. There are numerous designations of tinea based on where it appears on the body, though the same group of dermatophytes can cause any of tinea's presentations.

Tinea Infection	Common Name	Body Region Affected
tinea barbae	ringworm	beard area of the face
tinea capitis	ringworm	scalp
tinea cruris	jock itch	genitals
tinea corporis	ringworm	central trunk, arms, and legs
tinea pedis	athlete's foot	bottom of the foot and between the toes

Tinea is fairly contagious and spreads from person to person as well as through contact with surfaces, such as shower floors or soil, that can harbor the fungi. Dermatophytes can exist outside the body for a considerable length of time and thrive in environments that are warm and moist.

Symptoms and Diagnostic Path

The symptoms of tinea vary somewhat according to the part of the body affected, though generally include

- itching (PRURITUS), which may be intense, or PAIN
- redness (erythema)
- lesions that may appear as papules, vesicles, or plaques
- cracking or scaling of the lesions
- irregular HAIR loss (ALOPECIA) when the site of the infection is the scalp

The diagnostic path is generally straightforward. The doctor may take small scrapings of affected tissue to examine under a microscope. Such examination reveals the dermatophytes or evidence of their presence, which is conclusive for diagnosis. Inability to identify evidence of dermatophytes points to other causes for the symptoms.

Treatment Options and Outlook

Topical ANTIFUNGAL MEDICATIONS often effectively treat all forms of tinea except those involving the hair or NAILS. Prescription antifungal medications produce the most reliable results; over-the-counter products may require multiple applications. Because many people who acquire tinea continue the activities that resulted in exposure, reinfection is common. Pervasive or resistant tinea may require oral antifungal medications to attack the infection systemically. Oral antifungal therapy is necessary to eradicate tinea that involves the hair or the nails. Treatment may require up to eight weeks for some infections, particularly those involving the nails and the feet (tinea pedis).

COMMON ANTIFUNGAL MEDICATIONS FOR TREATING TINEA

econazole (topical)	fluconazole (oral)
griseofulvin (oral)	itraconazole (oral)
ketoconazole (topical and oral)	miconazole (topical)
naftifine (topical)	oxiconazole (topical)
sertaconazole (topical)	terbinafine (topical and oral)

Risk Factors and Preventive Measures

Common environmental settings in which dermatophytes thrive include communal showers, spas, and swimming pools. Wearing water socks or sandals when walking on wet surfaces helps protect the feet from contact with the fungi. Tinea can be an opportunistic infection in people who are IMMUNOCOMPROMISED, such as those taking IMMUNOSUPPRESSIVE THERAPY following ORGAN TRANSPLANTATION or who have HIV/AIDS.

See also ALOPECIA AREATA; CANDIDIASIS; DERMATITIS; ERYSIPELAS; FUNGUS; IMPETIGO; KERATINOCYTE; LESION; ONYCHOMYCOSIS; PAPULE; PSEUDOFOLLICULITIS BARBAE; PSORIASIS; TINEA VERSICOLOR; VESICLE.

tinea versicolor A fungal INFECTION of the SKIN that causes areas of altered pigmentation, usually darkened patches. Unlike other forms of TINEA,

tinea versicolor is not contagious. The FUNGUS responsible, *Malassezia furfur*, is normally present on the skin (NORMAL FLORA). Dermatologists do not know why the fungus causes infection in some people and not in others, though they suspect the infection is opportunistic in being able to gain a foothold when other challenges are occupying the IMMUNE SYSTEM. Treatment is typically a combination of topical and oral ANTIFUNGAL MEDICATIONS. As *M. furfur* is normal flora, tinea versicolor tends to recur in people who are susceptible to it. When recurrences are frequent, the dermatologist may prescribe prophylactic antifungal therapy.

See also VITILIGO.

tissue expansion A method for growing additional SKIN to use for autologous (self) skin grafts. Autologous grafts have the best rate of success when transplanted because they are native to the body and present no risk for graft rejection. Tissue expansion is a common method for many reconstructive surgery procedures, though requires adequate areas of healthy skin.

For tissue expansion, the surgeon makes a small incision to create a pouch or pocket in healthy skin and inserts a balloonlike pouch called a tissue expander. The surgeon then adds a small amount of saline, through a special valve, every few days or so over a period of several months. The expander encourages the skin to grow to cover it, slightly accelerating the rate of growth over that which would normally occur. When the new growth of skin reaches the desired surface area, the surgeon removes the expander and can harvest the skin to transplant elsewhere on the body. Tissue expansion grafts are highly successful for repairing skin surfaces damaged or lost to severe BURNS or injuries. Some HAIR TRANSPLANTATION methods also use tissue expansion to grow additional skin that contains healthy hair follicles.

As with any surgery, the primary risks associated with tissue expansion are INFECTION and excessive bleeding. The tissue expander generally creates a conspicuous bulge in the surface of the skin, though the skin profile at the growth site returns to normal when the surgeon removes the expander. The surgeon uses appropriate techniques to minimize scarring at the harvesting site as well as during placement of the new skin.

See also PLASTIC SURGERY.

toxic epidermal necrolysis A life-threatening inflammatory condition affecting the SKIN and underlying connective tissues, also called Stevens-Johnson syndrome. Toxic epidermal necrolysis usually results as an adverse DRUG reaction though may occur as a complication of INFECTION or CANCER. Doctors believe toxic epidermal necrolysis develops when an external event triggers the mechanism for programmed cell death (apoptosis), causing massive numbers of keratinocytes (the cells that primarily comprise the skin) to die. This in turn activates the body's IMMUNE RESPONSE, which attacks the dying cells. The massive death of keratinocytes results in large segments of skin sloughing off, leaving the underlying tissue exposed. Toxic epidermal necrolysis typically evolves over a period of 10 to 14 days, though once the skin eruptions begin deterioration is rapid.

Diagnosis is by skin biopsy, which shows the characteristic pattern of cell destruction and abundance of killer T-cells. In most situations the first line of treatment is plasmapheresis, a process somewhat similar to dialysis in which a mechanical BLOOD separator removes the serum and replaces it with donor serum. Plasmapheresis helps clear antibodies from the serum, reducing the immune response. Other treatments include frequent surgical débridement of skin surfaces, skin grafts to cover denuded surfaces, and precise fluid and electrolyte replacement.

Toxic epidermal necrolysis has a survival rate of about 60 percent. Those who survive often have long-term complications and face a challenging road to rehabilitation and recovery. The massive loss of skin causes extensive scarring similar to that of serious BURNS. The eyes also experience damage as the sloughing affects the conjunctiva and sclera (EYE tissues).

See also ADVERSE REACTION; ANTIBODY; HEMAPHERESIS; KERATINOCYTE; STAPHYLOCOCCAL SCALDED SKIN SYNDROME.

urticaria The clinical term for hives, an outbreak of wheals on the SKIN's surface. Acute urticaria, which comes on suddenly, typically signals a HYPERSENSITIVITY REACTION. The wheals contain fluid

the IMMUNE RESPONSE draws from the cells of the skin. They itch, often intensely (PRURITUS), and may appear and recede in various locations on the body (migration).

BREATHING difficulties with urticaria may indicate ANAPHYLAXIS, a life-threatening hypersensitivity reaction causing swelling of the airways that requires emergency medical care.

When urticaria manifests, the first focus is on subduing the response to relieve the symptoms and prevent complications. The doctor may administer an EPINEPHRINE injection to thwart a hypersensitivity response that appears to be intensifying or if the urticaria progresses. Most urticaria responds fairly quickly to ANTIHISTAMINE MEDICATIONS such as diphenhydramine (Benadryl) or hydroxyzine (Vistaril), which the doctor can administer by injection for severe urticaria. The wheals generally retreat within 6 to 8 hours and are entirely gone in about 36 hours with antihistamine therapy. Most people recover fully and can avoid future episodes by avoiding exposure to the substance that caused the reaction.

Potential complications associated with urticaria are uncommon though can be life-threatening. ANGIOEDEMA occurs when fluid accumulates in tissues other than the skin; most doctors consider it a progressive form of urticaria. Angioedema can affect internal structures, causing pressure and swelling that affects the ability of vital organs to function. When angioedema affects the airways it can cause BREATHING difficulties and ANAPHYLAXIS, the most serious hypersensitivity reaction. These complications occur only with repeat exposure to the substance causing the reaction.

Urticaria represents an IMMUNE RESPONSE in which the immune system releases IMMUNOGLOBULIN E (IgE), which causes mast cells to release HISTAMINE. The histamine draws fluid into the tissues. Numerous drugs, foods, environmental factors such as pollen and animal dander, and health conditions may cause urticaria. It is important to attempt to identify the causative factor to prevent recurrences. Hypersensitivity responses, which people also call allergic reactions, tend to intensify with repeated exposure to the substance.

A similar release of IgE occurs with chronic urticaria, as an immune-mediated response related to serious illnesses that challenge the immune system such as cancer. AUTOIMMUNE DISORDERS that affect the connective tissue, such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), AMYLOIDOSIS, and RHEUMATOID ARTHRITIS, can also cause chronic urticaria, as can exposure to extreme heat or cold. As with acute urticaria, treatment for chronic urticaria first targets symptom relief.

See also DERMATITIS; MAST CELL; WHEAL.

V

vesicle A small, blisterlike LESION on the SKIN that contains serous fluid. Vesicles typically occur in clusters and indicate INFECTION, such as with HERPES SIMPLEX VIRUS (HSV), or irritation, such as results from contact with poison ivy. Skin vesicles often hurt or itch. Treatment may include topical medications to relieve discomfort, with oral ANALGESIC MEDICATIONS (PAIN relievers) or ANTIHISTAMINE MEDICATIONS (to relieve itching) as necessary. Vesicles begin to recede and heal when the underlying circumstance causing them begins to resolve. Vesicles usually do not rupture or tear. During HEALING the body reabsorbs the serous fluid they contain, giving the appearance that the vesicles wither away until all that remains is a thin crust that eventually falls off.

In other contexts within the human body, a vesicle is a small saclike or pocketlike structure in an organ, such as the seminal vesicles in the male reproductive system.

See also BLISTER; BULLA.

vitiligo A condition of hypopigmentation in which melanocytes die in patches of SKIN, leaving macules that are pale and depigmented. Dermatologists believe vitiligo is an autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack melanocytes, the skin cells responsible for producing pigment. Vitiligo affects people of all races and ethic backgrounds, though is more conspicuous in people who have darker skin.

There appears to be no pattern to the presentation of vitiligo, which may affect small areas or nearly the entire skin surface. The depigmented areas have no other symptoms—that is, they do not cause itching or PAIN. Vitiligo occurs more frequently in people who have other AUTOIMMUNE DISORDERS such as ALOPECIA AREATA. Vitiligo is also associated with ADDISON'S DISEASE (a disorder of the ADRENAL GLANDS), HYPERTHYROIDISM, DIABETES, and pernicious ANEMIA.

Symptoms and Diagnostic Path

In most people who develop vitiligo, the areas of depigmentation generally appear slowly and start with small patches of skin. Some people do not develop more than a few such patches, while other people eventually develop large and numerous patches of depigmentation. In most people, the depigmentation is roughly symmetrical on both sides of the body, though in some people it affects only one side. The appearance of the depigmented areas is generally diagnostic as this is a unique symptom of vitiligo. The most common sites for depigmentation are the face, hands, arms, legs, and genitals.

Often there was a precipitating factor, such as a severe SUNBURN or other trauma to the skin, within several months of the start of symptoms. Serious physical injury or illness may also precipitate symptoms. The dermatologist may biopsy a representative LESION to rule out other causes. Sometimes blood tests will show the presence of antibodies, which strongly supports the diagnosis of an autoimmune disorder.

Treatment Options and Outlook

The cosmetic aspects of vitiligo are often the most disturbing feature of vitiligo for people who have the disorder, and most treatments target cosmetic improvement. Most aim to slow the progression of the depigmentation or to darken the appearance of depigmented areas and include topical CORTICOSTEROID MEDICATIONS, micropigmentation (therapeutic tattooing), and psoralen plus ultraviolet A (PUVA) PHOTOTHERAPY. Skin grafts are sometimes

an option for small areas of depigmentation, though are expensive and entail numerous risks. Cosmetics to cover depigmented areas work well for some people.

Another therapeutic approach is to create hypopigmentation consistently, lightening all of the skin using topical bleaching agents such as monobenzone to make the depigmented areas less conspicuous. Such lightening is permanent, and establishes heightened sensitivity to sun exposure with the risk for severe sunburn. The functional disturbances to the skin also have significant implications for health, as the depigmented areas cannot protect from sun damage. Protective, full-cover clothing and high sun-protection factor (SPF) sunscreens are necessary to provide this protection.

In most people, vitiligo progresses despite treatment. One of the most challenging dimensions to vitiligo, as with other dermatologic conditions that have similarly conspicuous symptoms, is the sense of social isolation and embarrassment many people who have the condition feel. Vitiligo is especially difficult for adolescents and young adults to manage. Support groups are often helpful for coping.

Risk Factors and Preventive Measures

Because dermatologists do not know what causes vitiligo to start, there are few known preventive measures. It does appear that significant trauma to the skin, such as a sunburn that blisters and peels, can trigger vitiligo. Most dermatologists believe GENE MUTATION is the underlying cause, as is the case with many autoimmune disorders, though researchers have yet to verify this. Limiting sun exposure by wearing protective clothing and sunscreen may slow the progression of vitiligo.

See also ALBINISM; ANTIBODY; MACULE; MELANOCYTE; TATTOOS.

W–X

wart A growth, typically rough and raised, that appears on the SKIN. The HUMAN PAPILLOMAVIRUS (HPV), which has numerous strains, causes common warts as well as variations including genital warts (a common sexually transmitted disease) and plantar warts which appear on the soles (plantar surfaces) of the feet. Because common warts are viral, physical contact can spread them to other locations on the affected person's body. However, common warts rarely spread to other people.

Symptoms and Diagnostic Path

Most common warts begin with a small, rough, raised bumps that can be the same color as the surrounding skin or discolored (typically pale). As they grow they take on the characteristic appearance of warts. Small dark dots sometimes appear inside the wart, which are clotted blood vessels though people commonly call them wart seeds. The "seed" of the wart is the HPV, and it is not visible. Warts seldom hurt or itch, though may do either as well as bleed when they are in locations that expose them to frequent irritation.

Treatment Options and Outlook

From a medical perspective, warts are harmless and do not require treatment. Because common warts continue to spread, however, it is prudent to remove them when they are small and few. Though the health consequence of warts is primarily cosmetic, warts that cluster in areas such as around the fingertips can create functional interference. Common therapies the dermatologist may use for removing warts include

- cryotherapy, such as treatment with liquid nitrogen, which freezes the wart
- electrodesiccation, which cauterizes or burns off the wart
- cantharidin, a topical chemical solution that forms a BLISTER which raises the wart from the skin
- topical salicylic acid, which chemically destroys the wart

Surgical remedies such as excision or laser therapy are effective and may be necessary for warts that resist other efforts, though they have substantially greater risks, including INFECTION and scarring. Oddly enough, an application of duct tape over the wart appears as successful as any other therapy for causing common warts to resolve. Most over-the-counter products for wart removal require multiple applications though are ultimately successful for those who are patient. Because they are viral, common warts tend to recur for as long as the HPV remains in the body, and HPV is extraordinarily difficult to eradicate.

Risk Factors and Preventive Measures

The risk factor for common warts is exposure to HPV, which is pervasive. Preventive measures include frequent and regular HAND WASHING and refraining from picking at or scratching existing warts. Prompt treatment to remove warts while they are small and restricted to a fairly contained area helps to limit their spread.

See also SCAR; SEBORRHEIC KERATOSIS; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; VIRUS.

wheal A raised, blisterlike LESION on the SKIN that usually results from an intradermal injection such as for allergy skin testing or the tuberculin skin test. Wheals also may occur in response to insect stings and topical allergic reactions (URTICARIA or

hives). Wheals associated with urticaria typically itch, sometimes intensely. Wheals usually do not rupture or tear, and gradually fade to smooth, red areas (macules) before disappearing entirely as the body absorbs the fluid they contain.

See also BULLA; MACULE; PRURITUS.

whitlow An INFECTION at the end of the finger, or less commonly the end of a toe, that contains pus and is very painful. The area is inflamed, enlarged, erythematous (reddened), and often oozing. A common cause of whitlow is infection with the HERPES SIMPLEX VIRUS (HSV), conveyed to the finger via contact with infectious secretions from oral herpes infections or genital herpes lesions. Some doctors use the terms *whitlow* and *paronychia* interchangeably, whereas others use whitlow to refer to HSV infection and paronychia to refer to bacterial infection. It is important to distinguish between the causes of the infection as the treatment approach is different. Herpetic whitlow features the vesicles characteristic of HSV infection, and treatment is primarily to relieve symptoms. Bacterial whitlow lacks vesicles and treatment requires ANTIBIOTIC MEDICATIONS.

See also ABSCESS; BACTERIA.

wrinkles Furrows or channels in the SKIN, typically resulting from repeated movements, such as facial expressions (for example, crow's feet and laugh lines), or from long-term exposure to sun and wind. Aging is the single-most significant factor that causes wrinkles. Wrinkles increase with age as the skin loses collagen and subsequently resiliency. As well, the skin and the cutaneous tissue layer that supports it both thin, providing less support.

People who have light-colored skin tend to have more wrinkles than people who have darker skin. Smoking ages the skin considerably, increasing the depth and number of wrinkles. Extensive wrinkles may signal substantial sun damage that is an alert for SKIN CANCER. Rapid or major weight loss also causes wrinkles, as the skin that stretched to accommodate the extra weight suddenly has no underlying support so it sags, bags, and wrinkles. Prematurely wrinkled skin has less ability to protect itself from the sun because its layers are thinner and contain fewer cells, which means less melanin to shield the skin from ultraviolet radiation.

For many people, wrinkles are cosmetically undesirable. Dermatologists offer a number of solutions to reduce the appearance of wrinkles. These include

- For a CHEMICAL PEEL, the dermatologist applies a caustic solution to the skin, causing the epidermis, and in a deep chemical peel the dermis, to slough away. The new skin that forms beneath is tighter, pulling the surface of the skin smooth.
- For DERMABRASION, the dermatologist mechanically removes the top layers of skin (with local Anesthesia), using a device similar to a small grinder or sander to strip away the epidermis.
- For LASER SKIN RESURFACING, the dermatologist uses a heat laser to "burn" away the top layers of the skin. This technique allows the dermatologist to precisely control the depth and extent of skin removal as well as to target some areas for deeper penetration and others for lighter penetration.
- For BOTULINUM THERAPY, the dermatologist injects purified botulinum toxin into the muscles beneath the skin. This paralyzes them and keeps them from contracting. The paralysis keeps the person from forming wrinkles. Botulinum therapy lasts three to four months on average, depending on the location and the person's natural skin-aging tendencies.
- For BLEPHAROPLASTY and RHYTIDOPLASTY, a surgeon performs cosmetic surgery operations to remove wrinkles and tighten the skin around the eyes (blepharoplasty) and the overall face (rhytidoplasty).

Though it is not possible to totally prevent wrinkles because they develop as a function of aging, it is possible to reduce their numbers and effects. Preventive measures include

- drink plenty of water to keep the skin well hydrated
- use topical moisturizers and emollients to hold moisture in the skin

- limit sun exposure, and wear protective clothing and sunscreen when outdoors
- stop smoking and avoid exposure to environmental cigarette smoke
- eat nutritiously, especially fruits and vegetables that supply B vitamins and vitamin C, antioxidants that may help prevent skin damage due to sun exposure

Numerous over-the-counter products and preparations purport to "cure" wrinkles. At best this is false advertising, as wrinkles are as inevitable as aging. However, products that add moisture and vitamins to the skin may be nonetheless beneficial for the skin.

See also AGING, INTEGUMENTARY CHANGES THAT OCCUR WITH; ANTIOXIDANT; LENTIGINES; SMOKING CESSATION; SURGERY BENEFIT AND RISK ASSESSMENT.

xanthoma A fatty deposit that forms a benign (noncancerous) LESION beneath the SKIN, though also may occur in other tissues. Xanthomas develop in people who have chronic, untreated HYPERLIPIDEMIA (elevated BLOOD cholesterol and triglycerides levels). In their most common form, xanthomas appear as yellowish blebs beneath the skin, typically rounded or oblong, that protrude as nodules or papules. Xanthomas that form on the eyelids, a common presentation, are xanthelasmas. Most xanthomas do not cause symptoms though may be cosmetically undesirable. Eruptive xanthomas may occur in clusters, typically occurring on the shoulders and inner surfaces of the arms, and often itch.

The most significant feature of xanthoma is the underlying lipid disorder, which signals increased risk for CORONARY ARTERY DISEASE (CAD) and HEART ATTACK. Many people who develop xanthomas have familial lipid disorders that result in unusually elevated levels of triglycerides and very low density lipoprotein cholesterol (VLDL-C) or low density lipoprotein cholesterol (LDL-C). These elevations are markers for serious CARDIOVASCULAR DISEASE (CVD) and require prompt medical treatment. Lowering the blood lipid levels helps prevent further xanthomas from developing, though has no effect on existing xanthomas.

A xanthoma may create functional interference depending on its location. Xanthelasmas on or near the eyelids can interfere with proper vision, for example, and xanthomas on the hands may cause irritation and PAIN during tasks that require manual dexterity. Many people choose to have xanthomas removed for cosmetic purposes. Several options are available for removing xanthomas, including cryotherapy (freezing), electrodesiccation (cauterizing), excision (cutting out), and LASER SURGERY. The site usually heals without scarring, although xanthomas tend to recur.

See also CHOLESTEROL BLOOD LEVELS; DIABETES; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; NODULE; PANCREATITIS; PAPULE; PRURITUS; RISK FACTORS FOR CARDIOVASCULAR DISEASE; TRIGLYCERIDE BLOOD LEVELS; XANTHELASMA.

THE NERVOUS SYSTEM

The NERVOUS SYSTEM directs the functions, voluntary and involuntary, of the body through an intricate network of specialized cells (neurons) that convey information in the form of electrochemical messages. Practitioners who diagnose and treat conditions of the nervous system are neurologists, neurosurgeons, and neuropsychiatrists. This section, "The Nervous System," presents a discussion of the structure of the BRAIN and nerves, an overview of neurologic functions in health and the disorders that occur as a result of physiologic (organic) dysfunction of the brain and nerves, and entries about the health conditions that can affect neurologic function.

Conditions involving the nervous system often directly involve other body systems as well. Entries for neuromuscular disorders and neuropsychiatric disorders in which the origins or symptoms are primarily neurologic appear in this section, "The Nervous System." Entries for neuromuscular disorders in which the origins or symptoms are primarily muscular appear in the section "The Musculoskeletal System." The section "Psychiatric Conditions and Psychological Issues" contains entries about disturbances of mood, emotion, personality, and mental health and illness.

Structures of the Nervous System

MENINGES
- dura mater
- arachnoid mater
- pia mater

BRAIN
- cerebral cortex (cerebrum)
- ventricles
- amygdala
- hippocampus
- thalamus
- HYPOTHALAMUS
- corpus callosum
- cerebellum
- brainstem
  - pons
  - medulla oblongata

CRANIAL NERVES
- first cranial NERVE pair: olfactory
- second cranial nerve pair: optic
- second cranial nerve pair: oculomoter
- fourth cranial nerve pair: trochlear
- fifth cranial nerve pair: trigeminal
- sixth cranial nerve pair: abducens
- seventh cranial nerve pair: facial
- eighth cranial nerve pair: vestibulocochlear
- ninth cranial nerve pair: glossopharyngeal
- tenth cranial nerve pair: vagus
- eleventh cranial nerve pair: accessory
- twelfth cranial nerve pair: hypoglossal

SPINAL CORD

SPINAL NERVES
- cervical (8 pairs, C1–C8)
- thoracic (12 pairs, T1–T12)
- lumbar (5 pairs, L1–L5)
- sacral (5 pairs, S1–S5)
- coccygeal (1 pair, CO1)

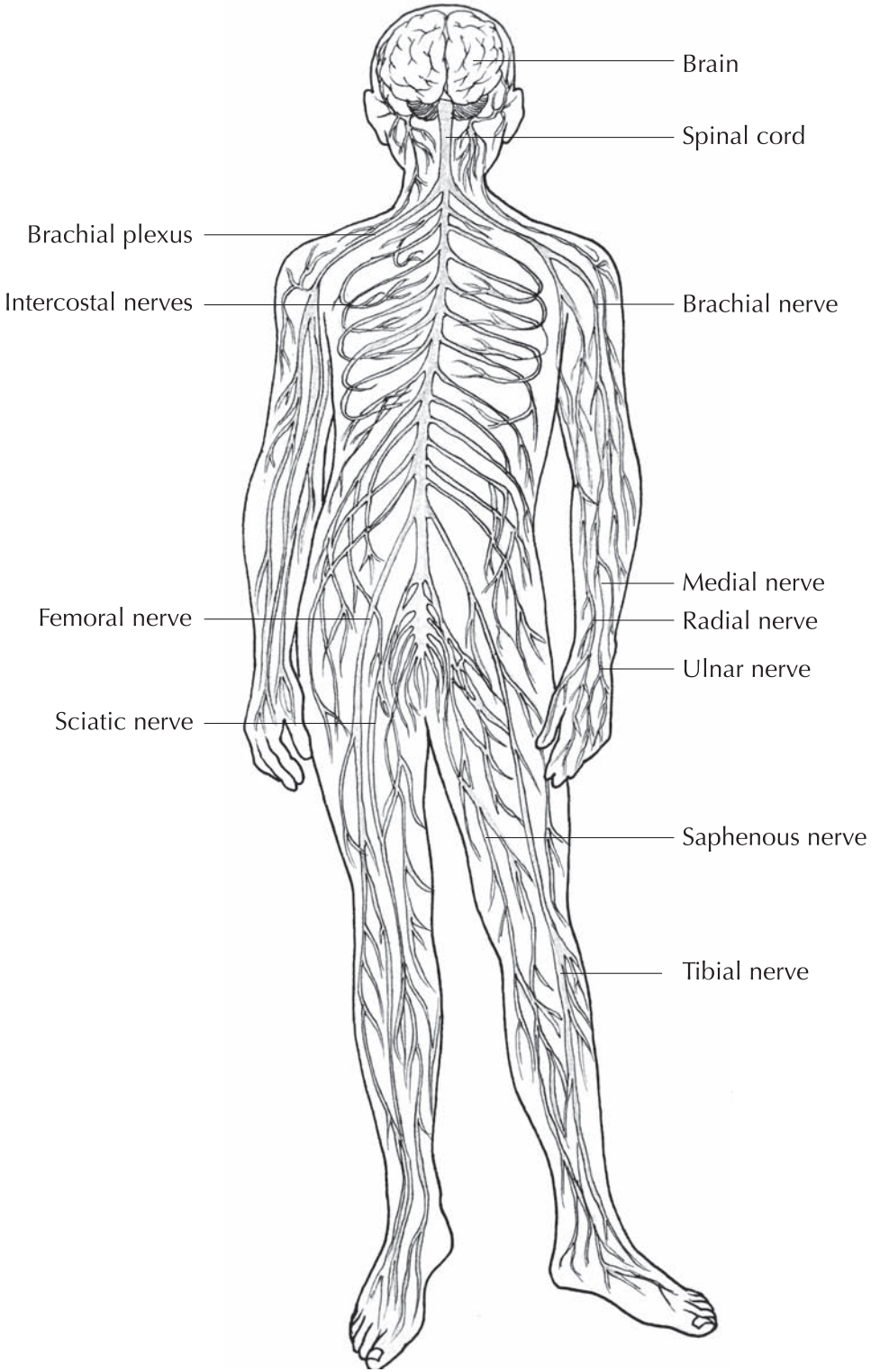
PERIPHERAL NERVES
- trunk
  - phrenic
  - intercostal
  - iliohypogastric
  - ilioinguinal
- arm
  - brachial
  - radial
  - musculocutaneous
  - medial
  - ulnar
- leg
  - femoral
  - sciatic
  - common peroneal
  - superficial peroneal
  - deep peroneal
  - tibial

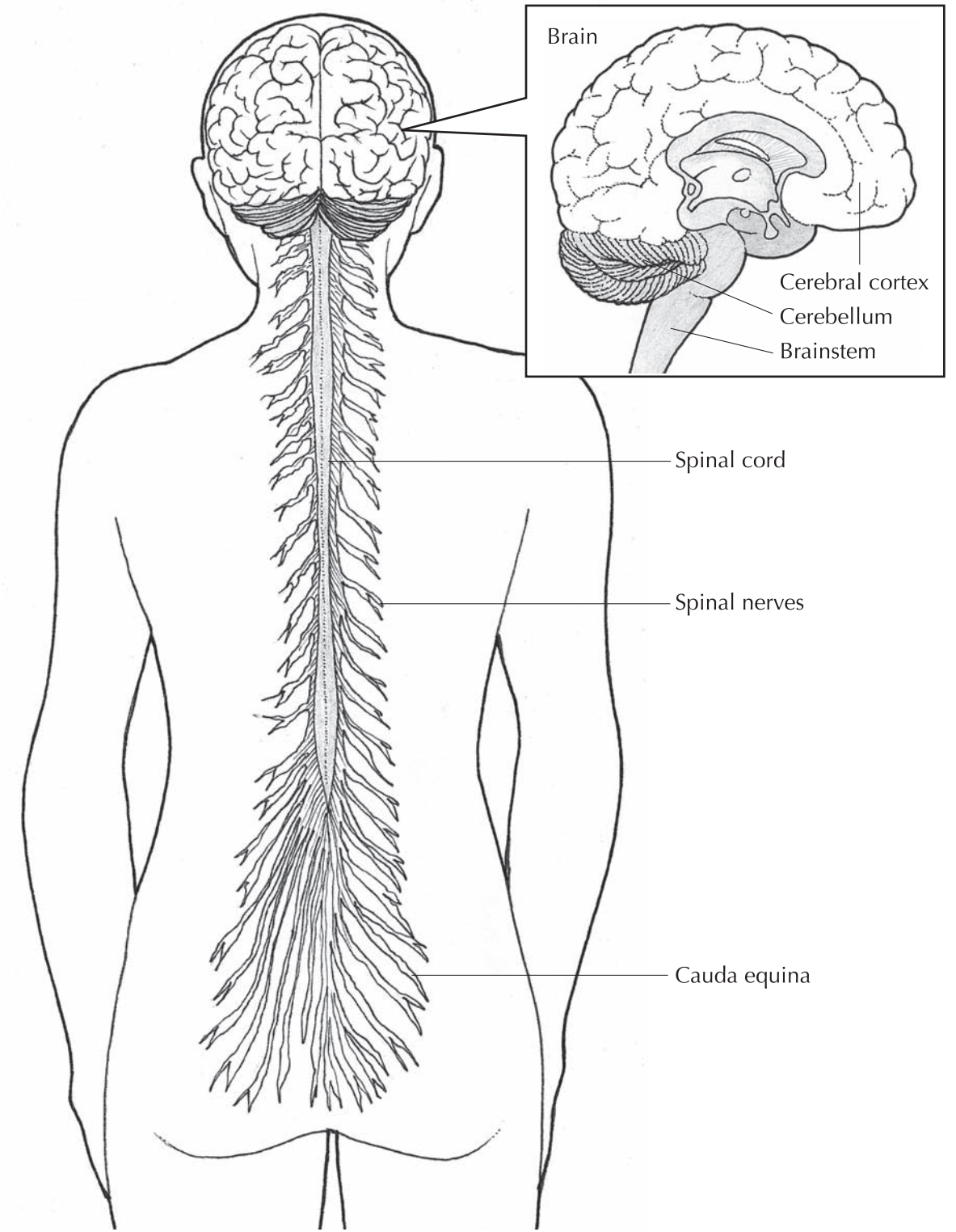
Functions of the Nervous System

The nervous system regulates and directs the functions of the body, processing billions of biochemical messages—bits of information traveling between the brain and the body—every minute. It is the earliest system to develop in the EMBRYO. The cells that will become the nervous system begin to separate and distinguish themselves about 14 days after CONCEPTION. During the following 7 days, the neural tube, the rudiment of the central nervous system, takes shape. By seven weeks of gestation, the neural tube has evolved into the SPINAL CORD and the brain. And by birth, the nervous system is anatomically complete.

The nervous system: organization and structure

Organized into a number of structural and func-


Brain
Spinal cord
Brachial plexus
Intercostal nerves
Brachial nerve
Medial nerve
Femoral nerve
Radial nerve
Ulnar nerve
Sciatic nerve
Saphenous nerve
Tibial nerve


Brain
Cerebral cortex
Cerebellum
Brainstem
Spinal cord
Spinal nerves
Cauda equina

tional divisions, the nervous system operates so efficiently that most of the time its myriad activities take place virtually unnoticed. The nervous system contains two major divisions: the CENTRAL NERVOUS SYSTEM and the PERIPHERAL NERVOUS SYSTEM.

The brain and spinal cord make up the central nervous system. The brain's main divisions are the cerebral cortex (cerebrum), cerebellum, and brainstem. The cerebral cortex is the largest and most complex part of the brain, accounting for 85 percent of the brain's mass and conducting all functions of consciousness and voluntary action. The cerebral cortex filters, sorts, and manages information about the body's experiences in its external environment. It is the center of thought, reason, intellect, emotion, judgment, personality, mood, behavior, and movement. The cerebral cortex also integrates many of the functions of other divisions of the nervous system and initiates voluntary movement.

CEREBRAL DOMINANCE

One or the other cerebral hemisphere is contralaterally dominant in nearly everyone. The most prominent feature of cerebral dominance is handedness. In about 85 percent of people, the left hemisphere of the cerebral cortex is dominant: they are right-handed (and usually right-footed and right-eyed). About 10 percent of people are right-hemisphere dominant: they are left-handed (and usually left-footed and left-eyed). About 5 percent of people appear to use either side of the body with equal ease: they are ambidextrous.

Structurally the cerebral cortex consists of two matched halves: the right hemisphere and the left hemisphere. A band of NERVE fibers, the corpus callosum, connects the two hemispheres at the bottom of the deep fissure that separates them. The functions of the hemispheres are contralateral to the body—that is, the right hemisphere controls the left side of the body and the left hemisphere controls the right side of the body. Matching pairs of lobes—frontal, temporal, parietal, and occipital—form the structure of each hemisphere, with each lobe specializing in certain functions. Though each pair of lobes handles similar operations, the right and left lobes conduct different aspects of those operations. Right hemisphere lobe operations tend to be spatial and conceptual, whereas left hemisphere lobe operations tend to be linear and logical. Regions of the frontal lobes work together to collect, assimilate, and integrate the results.

The cerebellum, a small structure at the back of the brain, coordinates motor function (movement). It receives a constant flow information from the cerebral cortex, the basal ganglia (a collection of nerve fibers on the basal, or bottom, surface of the cerebral cortex, where the planning and initiation of motor function takes place), the brainstem, and the body about the body's relationship to its external environment and sends in return a constant flow of instructions to seamlessly carry out tasks ranging from threading a needle to running a marathon. Like the cerebral cortex, the cerebellum has two hemispheres but operates ipsilaterally. The cerebellum manages balance, coordination, speed, direction, and the smoothness of movements.

The brainstem, an elongated, bulbous structure between the cerebral cortex and the spinal cord, maintains the functions of survival and connects the brain with the spinal cord. The primary structures of the brainstem are the pons, and midbrain, medulla oblongata. The pons functions as a bridge connecting the cerebellum, the cerebral cortex, and the spinal cord. The medulla oblongata is the segue from the brain to the spinal cord. It is responsible for the beating of the HEART, BREATHING, BLOOD PRESSURE, BLOOD flow, and many reflexes (automatic, survival-oriented reactions to environmental stimuli). The 2nd through the 12th pairs of CRANIAL NERVES originate in the brainstem. Injuries to the brainstem can be debilitating or fatal.

BILLIONS AND BILLIONS OF BRAIN CELLS

At the completion of its structural development just before birth, the BRAIN contains more than 100 billion neurons (NERVE cells) and about 50 times as many glial cells (cells that support the neurons). The longest neuronal axons, the threadlike fibers that carry nerve impulses away from the NEURON, reach from the brain to the base of the SPINAL CORD and extend nearly five feet in an adult.

The spinal cord, the body's largest nerve, is the thoroughfare of communication between the brain and the body. It extends from the second cervical vertebra to the second lumbar vertebra, a distance of about 20 inches in an adult. The bones of the spinal column, the vertebrae, enclose and protect the spinal cord. The spinal cord controls the reflexes of URINATION and defecation as well as of MUSCLE stretch (the automatic responses of muscle cells that allow movement).

All nervous system structures and functions outside the central nervous system belong to the peripheral nervous system: the cranial nerves, the spinal nerves, and their numerous branches. The 12 paired cranial nerves arise from the base of the brain and the brainstem. They convey sensory and motor signals to and from the structures of the head and face, one of each pair going to each side. The 31 paired spinal nerves branch from the spinal cord at each vertebra, carrying sensory and motor signals to and from the rest of the body.

Within the peripheral nervous system are two main subdivisions: the somatic nervous system, which handles voluntary functions such as movement, and the autonomic nervous system, which handles involuntary functions such as digestion. The autonomic nervous system has two further subdivisions. The sympathetic nervous system is made up of the nerves that serve the structures of the main trunk (thoracic and lumbar regions). The parasympathetic nervous system is made up of the nerves that serve the neck and head and the sacral region of the trunk.

DIVISIONS OF THE NERVOUS SYSTEM

CENTRAL NERVOUS SYSTEM: BRAIN and SPINAL CORD

PERIPHERAL NERVOUS SYSTEM: cranial nerves, SPINAL NERVES, and their branches

- somatic NERVOUS SYSTEM: voluntary functions
- autonomic nervous system: involuntary functions
  - † sympathetic nervous system: main trunk
  - † parasympathetic nervous system: head and sacral region

Nervous system communication: neurons, ions, and neurotransmitters The basic structure of function in the nervous system is the neuron, a specialized cell capable of sending and receiving electrochemical impulses that initiate or inhibit actions. What makes the neuron special are the filaments that extend from its cell body. A single such filament, the axon, extends from the cell body to carry nerve impulses from the neuron. From one to numerous other filamental processes, the dendrites, branch from other sites on the cell membrane to capture nerve impulses coming to the neuron. Like electrical wires, neurons would "short" if they came into contact with each other. Microscopic channels—synapses—help neurons keep safe distance from each other. Axons and dendrites reach toward, but do not touch, each other in the synapses.

WHITE MATTER AND GRAY MATTER

A fatty substance, myelin, coats most axons to insulate and protect them. The myelin gives the axons a whitish color. NERVE tissue in the BRAIN and SPINAL CORD, which is primarily a collection of axons, is white matter. The cell bodies of neurons are dark and grayish in color. Nerve tissue in the brain and spinal cord that is primarily a collection of NEURON cell bodies is gray matter.

Electrically charged chemical molecules—ions—are within and surround a neuron. Among the significant ions, sodium, potassium, and calcium are positive ions and chloride is a negative ion. Microscopic channels in the neuron's cell membrane, called ion channels, selectively allow ions to enter and leave the neuron. Each ion channel is specific for an ion—that is, calcium ion channels allow passage only of calcium ions and sodium ion channels allow passage only of sodium ions. When a neuron is at rest, the total charge of the ions within its membrane is negative relative to the ions outside its membrane. As well, there are more potassium ions within the cell body and more sodium ions outside the cell.

When a stimulus triggers an electrical impulse, the first stage of neuronal communication, the impulse causes sodium ion channels to open. Sodium ions rush into the neuron cell body, changing the neuron's polarity to become positive relative to the surrounding environment. The electrical impulse rides the wave of polarity down the axon of the sending neuron. About the time the impulse reaches the presynaptic terminals at the end of the axon, potassium ion channels open and potassium enters the cell body. In exchange,

because only so many ions can be inside the cell body, sodium ions leave. To restore itself to negative polarity the cell body activates a burst of energy to "pump" more sodium ions out, at an exchange rate of three sodium ions out for every two potassium ions in.

Meanwhile, back at the synaptic terminals another conversion is taking place. The synaptic terminals contain tiny storage pockets called vesicles that hold NEUROTRANSMITTER molecules. The electrical impulse causes the synaptic vesicle to release a neurotransmitter molecule. The neurotransmitter molecule crosses the synapse and binds with a NEURORECEPTOR on a dendrite of the receiving neuron. The binding either causes or blocks an action.

The longer the neurotransmitter molecules remain in the synapse the more neuroreceptors they can bind. As a safety mechanism, the neurotransmitter's presence in the synapse stimulates the synaptic vesicles to reuptake (recycle) the remaining neurotransmitter, containing the potential for binding. Further stimuli are then necessary to continue. The neuron sending a message is the presynaptic neuron; the neuron receiving a message is the postsynaptic neuron. Some neurologic conditions affect the functioning of presynaptic neurons and others affect the functioning of postsynaptic neurons.

NEURONAL PATHWAYS: THE BRAIN'S ENDLESS CAPACITY TO LEARN

The adult BRAIN contains 60 to 200 trillion synapses. Synapses represent the networks of axons that neurons develop to form neuronal pathways, the routes by which neurons communicate with one another in expedited fashion. Even though all the neurons the brain will ever have are present at birth, the brain has an endless capacity to create new neuronal pathways and thus "grow" its ability to learn.

Many medications work by inhibiting (blocking) or expediting the reuptake process to extend or shorten, respectively, the time the neurotransmitter is active. Selective serotonin reuptake inhibitors (SSRIs), for example, are ANTIDEPRESSANT MEDICATIONS that work by blocking serotonin reuptake. Serotonin is a neurotransmitter that facilitates neuron communication in areas of the brain related to mood. The acetylcholinesterase inhibitors, medications to treat ALZHEIMER'S DISEASE, work by blocking the enzyme that breaks down the neurotransmitter acetylcholine. This action extends the presence of acetylcholine in the synapses, increasing neuroreceptor binding. Acetylcholine facilitates neuron communication in areas of the brain that process cognitive functions and memory. Medications may also masquerade as neurotransmitters to bind with neuroreceptors. Therapies for PARKINSON'S DISEASE, a degenerative condition that results from depletion of the neurotransmitter DOPAMINE in the brain, are among the most effective applications of this approach.

Health and Disorders of the Nervous System

The most significant health risks the nervous system faces occur before birth. The most vulnerable period in nervous system development takes place before most women have missed a menstrual period or suspect they are pregnant. Within the first three weeks after conception, the rudimentary nervous system, the neural tube, forms and rapidly differentiates into the brain and spinal cord. Numerous factors, environmental and genetic, can disrupt this process to cause cephalic disorders (structural defects of the brain) or SPINA BIFIDA (structural defects of the spinal cord). CEREBRAL PALSY is the most common developmental disturbance of the nervous system.

FOLIC ACID AND NEURAL DEVELOPMENT

Folic acid is crucial for proper development of the NERVOUS SYSTEM early in PREGNANCY, especially at the time of CONCEPTION through the first trimester. Numerous studies show that taking folic acid supplements before and during pregnancy can prevent 70 percent of NEURAL TUBE DEFECTS. Health experts recommend that all women of childbearing age take 400 micrograms of folic acid supplement daily regardless of whether they are trying actively to become pregnant.

From birth through midlife, injury becomes the most worrisome threat to the nervous system. Young people are especially vulnerable to TRAUMATIC BRAIN INJURY (TBI) and SPINAL CORD INJURY; 80

percent of spinal cord injuries occur in people who are between the ages of 15 and 30. Many of these ACCIDENTAL INJURIES are preventable. Many of the illnesses that threatened not only nervous system function but often life itself—POLIOMYELITIS, ENCEPHALITIS, MENINGITIS—in previous generations are now either preventable or treatable.

HEALTH CONDITIONS INVOLVING THE NERVOUS SYSTEM

ALZHEIMER'S DISEASE	AMYOTROPHIC LATERAL SCLEROSIS (ALS)
APHASIA	ATAXIA
APRAXIA	AUTISM
ATHETOSIS	BRAIN TUMOR
BELL'S PALSY	CEREBRAL PALSY
BRAIN HEMORRHAGE	cognitive dysfunction
CHOREA	DELIRIUM
CONCUSSION	developmental disabilities
DEMENTIA	ENCEPHALITIS
DYSKINESIA	GUILLAIN-BARRÉ SYNDROM
ENCEPHALOPATHY	HERNIATED NUCLEUS PULPOSUS
HEADACHE	HYDROCEPHALY
HUNTINGTON'S DISEASE	memory impairment
LEARNING DISORDERS	MULTIPLE SCLEROSIS
MENINGITIS	MYOCLONUS
MYASTHENIA GRAVIS	NARCOLEPSY
MYOTONIA	NEURAL TUBE DEFECTS
NEURALGIA	NEUROFIBROMATOSIS
NEURITIS	ORGANIC BRAIN SYNDROME
NEUROPATHY	PARESTHESIA
PARALYSIS	POLIOMYELITIS
PARKINSON'S DISEASE	SEIZURE DISORDERS
RESTLESS LEGS SYNDROME	SPINAL CORD INJURY
SPINA BIFIDA	TOURETTE'S SYNDROME
TIC	TREMOR DISORDERS
TRAUMATIC BRAIN INJURY (TBI)	

Systemic health conditions shift to the forefront of concern with the approach of late age. CARDIOVASCULAR DISEASE (CVD), endocrine disorders, pulmonary disease, and disorders of METABOLISM arising from LIVER and kidney disease become more prevalent with advancing age. All of these conditions have the potential to affect nervous system function. STROKE, a consequence of cardiovascular disease, is the leading cause of disability resulting from damage to the brain. Metabolic disorders such as chronic CIRRHOSIS and DIABETES may disrupt the body's biochemical balances to the extent of creating brain dysfunction (ENCEPHALOPATHY). Health conditions that directly affect the nervous system also become more frequent with increasing age. The most common—and disabling—such conditions are Alzheimer's disease, Parkinson's disease, and DEMENTIA. Alzheimer's disease alone affects as many as 50 percent of people age 85 and older.

Traditions in Medical History

The earliest medical writings of Eastern and Western physicians document nervous system conditions such as epilepsy (SEIZURE DISORDERS) and surgical treatments that involved boring through the skull, probably to relieve pressure resulting from head trauma. Healed wounds in skulls, clearly made by intent, remain as archaeological evidence that physicians of antiquity were somewhat sophisticated, as well as successful, in their methods. Mummified remains reveal that poliomyelitis—which approached worldwide eradication in 2005 through vaccination efforts, with the exception of a few pockets where the disease remained endemic—was fairly common among ancient Mesopotamians and Egyptians.

The Greek physician and philosopher Hippocrates, the father of modern medicine, was the first to determine the brain's responsibility for consciousness and control of the body. The inability to directly explore the structure and function of the brain resulted in centuries of misunderstandings, however. The first accurate representations emerged when in 1543 Andreas Vesalius (1514–1564) published the landmark manuscript *De humani corporis fabrica libri septum,* more familiarly known today as *The Fabric of the Human Body*. The manuscript presented the first drawings of the human brain based on dissection and physical examination.

Breakthrough Research and Treatment Advances

Today some of the greatest advances in understanding of brain and nervous system structure and function come from research in genetics and molecular medicine. HUNTINGTON'S DISEASE was one of the first neurologic disorders for which researchers established a conclusive genetic foundation. In the 1990s researchers uncovered mutations in genes responsible for Parkinson's disease, Alzheimer's disease, and Lewy body dementia.

There is great hope that such discoveries will lead to effective treatments for these and other degenerative neurologic conditions.

Other research focuses on replacing lost or damaged nervous system tissue. STEM CELL transplantation, still experimental, shows promise for treating conditions such as Parkinson's disease, Alzheimer's disease, MULTIPLE SCLEROSIS, AMYOTROPHIC LATERAL SCLEROSIS (ALS), and spinal cord injury. Researchers are also combining GENE and molecular technologies to cultivate neurons in the laboratory with the hope of providing additional sources of transplantable cells.

Other breakthroughs involve new understanding about how the brain functions. Highly sophisticated imaging technologies such as POSITRON EMISSION TOMOGRAPHY (PET) SCAN and SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) SCAN allow researchers to observe changes in the brain during brain activity. Such observations have provided insights into the processes of memory and cognitive function and offer an objective means for assessing the effectiveness of therapeutic approaches for neurologic disorders such as Alzheimer's disease, Parkinson's disease, and seizure disorders.

In the 1980s scientists discovered the brain has the ability to reorganize the way it functions to some degree, allowing different areas of the brain to take over for certain areas that become damaged. Whether this process permits the brain to default to abandoned pathways or to create new pathways remains unknown. Researchers continue to explore the mechanisms of this reorganization, hopeful that further discoveries will lead to therapies to retrain the brain after stroke or traumatic brain injury and perhaps to compensate for functional losses due to disease processes such as those that occur with multiple sclerosis and Alzheimer's disease.

A

aging, neurologic changes that occur with A rudimentary NERVOUS SYSTEM is among the first structures to form as a new life begins. The CENTRAL NERVOUS SYSTEM begins to form about two weeks after CONCEPTION, arising from a cluster of specialized cells called the ectoderm. Its physical and functional development is about 60 percent complete by birth, 80 percent complete by age three, and finally reaches completion at the end of ADOLESCENCE. Though the full complement of neurons is in place by early childhood, the BRAIN continues to establish new pathways for NEURON communication for most of life.

The Prenatal Nervous System

The first recognizable neurologic structure is apparent 21 days after conception when the cells of the ectoderm grow and divide to form the neural tube, a primitive structure of NERVE tissue. Over the following four weeks the neural tube elongates and closes at each end to form the SPINAL CORD and the brain, a process called neuronal migration. This is one of the most sensitive times in embryonic development. NEURAL TUBE DEFECTS—such as SPINA BIFIDA and anencephaly, which result when one or the other end of the neural tube fails to close—are among the most common BIRTH DEFECTS involving the nervous system.

The brain grows by 50,000 neurons a second during most of this migration period, forming the brain's three major divisions—prosencephalon (forebrain), mesencephalon (midbrain), and rhombencephalon (hindbrain)—which themselves grow and divide to form the core structures of the brain. From the spinal cord, the SPINAL NERVES and PERIPHERAL NERVES begin to tendril out to the organs and structures of the body, establishing motor and sensory innervations that will carry nerve impulses to and from the body throughout life.

The Early Childhood Nervous System

The brain continues to add new cells at an astonishing rate, doubling in size from birth by the time a child reaches 18 months of age. Intense learning takes place during this period, during which the brain acquires the foundations of language, sensory interpretation, and motor skills. Interruptions of these processes can have serious and lifelong consequences. Studies with animals show, for example, that depriving the brain of visual input during the time the brain is establishing the pathways for interpreting visual signals results in permanent blindness even though the structural components of vision—the EYE, OPTIC NERVE, and brain regions—are intact.

Throughout childhood brain neurons continue to expand the connections they make with each other, laying down the hundreds of thousands of pathways necessary for learning and remembering. These neuronal networks provide shortcuts that allow the brain to carry out familiar functions with great speed and efficiency. The foundations of language and motor movement develop and evolve during this period of expansion. Though researchers agree it is never to late for the brain to learn, it is during the years of childhood that the brain is most receptive.

The Adolescent Nervous System

During adolescence (between the ages of 12 and 20) axons continue to grow and branch, most notably from the neurons of the frontal lobes, which are responsible for many of the functions of cognition and behavior, and to lesser extent from neurons in other areas of the brain. This is the

final stage of functional organization of the brain's processes and mechanisms. The numbers of neuroreceptors on the surfaces of neurons also increase dramatically, particularly those for DOPAMINE which is the primary brain NEUROTRANSMITTER for functions of cognition and behavior. This axonal growth makes the adolescent brain especially vulnerable to the neurotoxic effects of ALCOHOL and drugs. Damage that disrupts axonal growth during adolescence often has complex and permanent, consequences for brain function during the rest of life.

The Elderly Nervous System

The brain remains capable of carrying out its functions across the lifespan unless injury or disease interrupts. But by old age the likelihood of injury, disease, and general health problems is higher than any other stage of life. Many diseases common in old age affect the brain and nervous system even when they primarily involve other body systems. CARDIOVASCULAR DISEASE (CVD), for example, may change the BLOOD flow to the brain. HYPERTENSION (high BLOOD PRESSURE), one of the most common forms of cardiovascular disease, is the leading cause of STROKE; and stroke is the leading cause of disabling brain injury. DIABETES damages the delicate blood vessels that nourish the peripheral nerves, most notably damaging sensory perception—the ability of distant body parts such as the feet to send PAIN signals to the brain (peripheral NEUROPATHY). Chronic CIRRHOSIS creates widespread metabolic imbalances in the body that alter brain functions from cognition to motor movement (hepatic ENCEPHALOPATHY).

The likelihood of neurologic disease also increases with age. Conditions such as ALZHEIMER'S DISEASE, PARKINSON'S DISEASE, HUNTINGTON'S DISEASE, DEMENTIA, CREUTZFELDT-JAKOB DISEASE (CJD), TREMOR DISORDERS, and ORGANIC BRAIN SYNDROME seldom develop in people under the age of 50. As many as half those age 85 and older have Alzheimer's disease, however. Progressive neurologic conditions that begin earlier in life, such as MULTIPLE SCLEROSIS, tend to exhibit the most severe of their symptoms as age advances. Such changes are generally irreversible.

Neurons, like other cells, die throughout life. Researchers believe such cell death is a form of culling that helps the brain maintain its efficiency. By old age the cumulative effect of this cell death results in decreased brain tissue. Imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) show the ventricles (spaces) are larger in the brain of a 70-year-old person than a 30-year-old person. The numbers of sensory nerve receptors in the body (peripheral nerve structures) also begin to decline, reducing to some extent the sensory input that reaches the brain.

But these changes are not sufficient, in themselves, to significantly diminish the brain's functions. Indeed, recent research suggests the brain gets "smarter" with age, developing shortcuts and efficiencies in the ways that it processes information. Many people reach age 80 and beyond with relative good memory, cognition, and independence. Though physical changes do take place in the brain with aging, researchers believe neurologic deficiency is *not* inherently a normal dimension of aging.

See also CEREBRAL PALSY; COGNITIVE FUNCTION AND DYSFUNCTION; FETAL ALCOHOL SYNDROME; MEMORY AND MEMORY IMPAIRMENT.

Alzheimer's disease A progressive, degenerative condition that causes irreversible loss of cognitive and memory functions. The hallmarks of the disease are the diminished production of acetylcholine, a NEUROTRANSMITTER essential for cognitive function, and the formation of amyloid plaques (abnormal protein deposits) and neurofibrillary tangles (resulting from another protein, tau), within the BRAIN. These formations interfere with normal NEURON communication and literally "scramble" NERVE signals. Alzheimer's disease is typically a condition of aging, primarily affecting people age 70 and older, though an early-onset form of the disease may strike people who are in their 40s or 50s. Early-onset Alzheimer's disease tends to progress more rapidly. More than 4 million Americans have Alzheimer's disease.

The causes of Alzheimer's disease remain unclear, though GENE MUTATION is emerging as a leading candidate. In the 1990s researchers correlated mutations in the apolipoprotein E (apoE) gene on CHROMOSOME 19 with the tendency, depending on the ALLELE (form of the gene) inherited, to develop Alzheimer's disease in old age.

People with one allele pairing appear less likely to develop the disease, and those with other allele pairings seem more likely. Researchers believe there are other genes that may affect a person's GENETIC PREDISPOSITION for Alzheimer's disease, though developing the disease is an interaction among environmental factors, such as the individual's overall health status and lifestyle habits, and genetic factors.

Early-onset Alzheimer's disease, in which symptoms appear before the age of 60 (often in the 40s and 50s), is the only form of Alzheimer's disease researchers know for certain is hereditary. It occurs as a result of mutated genes on chromosomes 1, 14, and 21 that cause alterations in proteins that have key functions in the brain in regard to regulating amyloid. The mutations occur in an autosomal dominant INHERITANCE PATTERN, which means each child of a person who has the gene mutation has a 50 percent chance of inheriting the gene. In this form of Alzheimer's disease, also called familial Alzheimer's disease, it appears that inheriting any one of the mutated genes establishes the certainty of developing the disease. Researchers are sure that variables of personal health play a significant role in whether any given individual develops the disease, though they do not yet know what those variables are.

Symptoms and Diagnostic Path

Early symptoms of Alzheimer's disease tend to be vague and inconsistent deviations from the known and familiar. Though memory loss is the most familiar symptom, it is more than simply misplacing one's car keys or forgetting an appointment. A person may travel the same route to and from the store, for example, and then become completely lost. Early symptoms that can suggest Alzheimer's disease include

- confusion when following directions
- forgetting familiar people and places
- inability to write a check or count out money to pay for purchases
- repeatedly asking the same questions or telling the same information
- inability to prepare meals or perform common household tasks
- stops speaking in the middle of sentences or conversations

Later symptoms become more pronounced and limit independent functioning. Later symptoms of Alzheimer's disease include

- DEMENTIA
- forgetting to eat or drink
- engaging in socially inappropriate behavior such as public MASTURBATION
- disorientation
- inability to recognize people and places and sometimes self

The diagnostic path includes a comprehensive medical examination, thorough NEUROLOGIC EXAMINATION, ELECTROENCEPHALOGRAM (EEG), and usually imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN to rule out other possible causes (such as BRAIN TUMOR or STROKE) that could cause the symptoms.

Diagnosis of Alzheimer's disease is primarily clinical, as only examination of brain tissue at autopsy following death can provide definitive evidence of the hallmark amyloid plaques and neurofibrillary tangles. The person's age, the gradual progression of symptoms, and ruling out other possible causes of the symptoms lead the neurologist to the diagnosis of Alzheimer's disease. POSITRON EMISSION TOMOGRAPHY (PET) SCAN and SINGLE-PHOTON EMISSION TOMOGRAPHY (SPECT) SCAN often can show the progression of damage within the brain as Alzheimer's disease advances. This can help confirm the diagnosis and monitor the effectiveness of medications in slowing the deterioration.

Treatment Options and Outlook

In the 1990s the US Food and Drug Administration (FDA) approved a new class of drugs, acetylcholinesterase inhibitors, to treat Alzheimer's disease. These drugs, such as donepezil (Aricept) and rivastigmine (Exelon), prevent the enzyme acetylcholinesterase from metabolizing (breaking down) acetylcholine. This action extends the length of time acetylcholine remains available to neurons, compensating to a certain degree for the diminishing amounts of acetylcholine the brain

produces as Alzheimer's disease progresses. Eventually acetylcholine production drops below the level at which extending its presence is useful, however, making these medications most effective in the early to middle stages of the disease.

There is some evidence that GINKGO BILOBA, a botanical supplement, improves the cognitive and memory symptoms of early to middle Alzheimer's disease in some people. Ginkgo biloba has no known effect on neurotransmitters directly; its action appears to be that it improves the circulation of BLOOD throughout the brain. This possibly broadens the areas of the brain that participate in cognitive functions. However, ginkgo biloba also affects COAGULATION (the processes of clotting). People who take anticoagulant medications, including daily ASPIRIN THERAPY, should not take ginkgo biloba unless their doctors approve and determine there are no interactions likely with prescribed medications.

Other treatments for Alzheimer's disease are primarily supportive and may include OCCUPATIONAL THERAPY to provide methods for maintaining cognitive function and memory for as long as possible. Activities that use these functions, such as crossword puzzles and reading, seem helpful. Some studies show that daily physical exercise, such as walking, slows the progression of Alzheimer's disease, though the mechanisms through which it may do so remain unknown.

Alzheimer's disease is challenging and emotionally draining for family members and friends who participate in caregiving. Most people want to maintain their loved ones at home for as long as possible, such that it often takes a traumatic event to force the recognition that the person requires more extensive care. Specialized Alzheimer's care facilities provide the staffing and environment to keep the person with Alzheimer's disease safe. SUPPORT GROUPS for family members and caregivers provide forums for sharing information and understanding. Because Alzheimer's disease is progressive and incurable, it is important for families to discuss key END OF LIFE CONCERNS with the person before impairment becomes significant. Most people prefer to make decisions about their own care and are more comfortable when they can feel confident their desires will shape the care they receive.

Risk Factors and Preventive Measures

Age is the primary risk factor for Alzheimer's disease. Though researchers have investigated numerous apparent correlations between environmental exposures (such as to aluminum) and Alzheimer's disease, they have not been able to substantiate them. Genetic factors are likely significant contributors. Except for early-onset Alzheimer's disease, however, the role of the genetic component of Alzheimer's disease remains uncertain. Researchers discovered in the early 2000s that people taking statin medications (such as lovastatin) to lower blood cholesterol levels have a much lower rate of Alzheimer's disease than people who do not take these medications, and they continue to investigate what correlations may exist.

At present, however, there are no measures known to prevent Alzheimer's disease. Because environmental factors such as overall personal health, nutrition, and lifestyle likely contribute in some fashion to conditions that allow Alzheimer's disease to develop, health experts encourage nutritious EATING HABITS, daily physical activity, and other lifestyle measures to maintain optimal health.

See also AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; COGNITIVE FUNCTION AND DYSFUNCTION; LIFESTYLE AND HEALTH; MEMORY AND MEMORY IMPAIRMENT.

amnesia See MEMORY AND MEMORY IMPAIRMENT.

amyotrophic lateral sclerosis (ALS) A progressive, degenerative disorder in which motor neurons (NERVE cells in the SPINAL CORD that are responsible for movement) die, resulting in loss of voluntary MUSCLE function. ALS does not affect involuntary muscle function or other neurologic structures. Other names for ALS include Lou Gehrig's disease, Charcot's disease, and motor NEURON disease. ALS affects half again as many men as women and typically appears in people who are between the ages of 40 and 60.

Though ALS ultimately affects all voluntary muscle function, it typically begins in one of the three types of motor neurons:

- upper motor neurons, which regulate voluntary muscle function in the upper extremities

- lower motor neurons, which regulate voluntary muscle function in the lower extremities
- bulbar motor neurons, which affect the functions of structures in the BRAIN that regulate coordination of movement throughout the body

As motor neurons die the muscles they control can no longer function. As ALS progresses and muscle cells become inactive, the muscles atrophy (waste away). These events in combination result in the debilitating loss of mobility. Regardless of the disease's point of origin, it eventually affects all voluntary muscles in the body. Because the bulbar structures in the brain additionally have functions related to emotion, loss of emotional control is also common particularly in the disease's later stages. Researchers do not know what causes motor neurons to die, nor do they know the precise mechanisms by which cell death occurs.

Symptoms and Diagnostic Path

The development of symptoms varies with the first location of motor neuron loss. Early symptoms of ALS are generally vague, sporadic, and asymmetrical (one-sided). Among them are

- muscle cramps
- emotional inappropriateness and lability (mood swings)
- difficulty speaking, notably slurred speech
- excessive salivation (SIALORRHEA) and difficulty swallowing

Symptoms gradually progress, often over the course of several years, to a level at which they interfere with normal activities. The diagnostic path generally starts with BLOOD tests to assess thyroid and parathyroid function and to detect any presence of heavy metals, notably lead. HYPERTHYROIDISM, HYPERPARATHYROIDISM, and lead poisoning can cause symptoms similar to those of ALS. The diagnostic path also includes electromyography (EMG) to assess muscle function in affected as well as unaffected limbs. The neurologist may further conduct diagnostic imaging procedures of the brain and spinal cord, such as MAGNETIC RESONANCE IMAGING (MRI) of the cervical spine, to rule out other causes of the symptoms. There are no definitive diagnostic tests for ALS.

LOU GEHRIG'S DISEASE

Amyotrophic lateral sclerosis (ALS) struck American baseball legend Lou Gehrig (1903–1941) at the height of his record-setting career. After Gehrig struggled for more than a year with the progressive loss of neuromuscular function characteristic of ALS, doctors made the diagnosis. Gehrig remained a public figure even as his health deteriorated, drawing attention to the disease that finally claimed his life at the age of 38. Americans more familiarly know ALS as Lou Gehrig's disease. However, French neurologist Jean-Martin Charcot (1825–1893) first described the symptoms of this rare condition in 1869. Doctors in France and much of Europe refer to ALS as Charcot disease.

Treatment Options and Outlook

At present treatment for ALS is primarily supportive; there is no cure. The medication riluzole, which blocks release of the NEUROTRANSMITTER glutamate, often can slow the progression of symptoms. Glutamate stimulates activity in the brain, which correspondingly increases nerve signals to parts of the body such as the muscles. People who have ALS tend to have elevated blood levels of glutamate, and some research suggests glutamate overstimulation may damage motor neurons. Researchers do not know what causes the elevation, however, or whether it contributes to or results from the ALS. The neurologist may prescribe other medications such as baclofen and tizanidine to treat muscle spasms and anticholinergic medications to control excessive salivation.

The progressive loss of muscle control eventually affects vital functions such as swallowing, which affects the ability to eat, and BREATHING. Important treatment decisions as ALS progresses include choices around the insertion of a permanent feeding tube, called a percutaneous endoscopic gastrotomy (PEG) tube, to provide adequate nutrition and assistive breathing devices, including MECHANICAL VENTILATION. Some people who have ALS choose full support to extend life as long as possible and others opt for only those supportive

measures that provide the QUALITY OF LIFE that is acceptable to them. Treatment decisions are uniquely individual.

About 40 percent of people who have ALS live 5 to 10 years after diagnosis, and 10 percent survive longer than 10 years. Pulmonary failure and its complications are usually the cause of death. Because ALS is a fatal disease, those who have it should discuss their treatment preferences and END OF LIFE CONCERNS with their physicians and family members, and establish their desires in writing through advance directives such as medical power of attorney and living will.

Risk Factors and Preventive Measures

ALS appears to be familial (hereditary) in about 20 percent of people who develop it, occurring in an autosomal dominant INHERITANCE PATTERN. Neurologists classify the remaining 80 percent as sporadic. Family history is the strongest individual risk factor for developing ALS. Epidemiologists can identify trends in which pockets of ALS occur, suggesting there are common risk factors for sporadic ALS. As yet no clear evidence has emerged that identifies these risk factors or that establishes any explanation for why only a small percentage of people exposed to the same circumstances develop ALS. Some research suggests ALS may have components of autoimmune and mitochondrial dysfunction, though the causes and mechanisms of ALS remain unknown. There are no known measures to prevent ALS.

See also APOPTOSIS; AUTOIMMUNE DISORDERS; CRAMP; GUILLAIN-BARRÉ SYNDROME; HEAVY-METAL POISONING; MITOCHONDRIAL DISORDERS; MULTIPLE SCLEROSIS; MYASTHENIA GRAVIS; SPASM; STROKE.

aphasia Loss of the ability to use language. Aphasia results from damage to the areas of the BRAIN responsible for language, often due to STROKE. Because these areas of the brain are functional rather than structural, doctors cannot predict the extent to which injury will affect language. Other causes of aphasia include BRAIN TUMOR and TRAUMATIC BRAIN INJURY (TBI). Aphasia sometimes occurs in the later stages of neurodegenerative disorders such as ALZHEIMER'S DISEASE and PARKINSON'S DISEASE. It may involve any individual aspect or combination of aspects of the abilities to speak, read, write, and understand language.

In most people the left brain contains the functional centers responsible for speech and language, so stroke or other injury affecting the left brain may produce aphasia, ranging from limited (certain kinds of words or expressions) to global (complete inability to communicate through language). These functional centers conduct all brain activity related to language concepts, including expression such as through SIGN LANGUAGE, not only through speech. Severe damage to these centers appears to prevent the person also from engaging in pantomime and other methods of communication, creating significant disability.

People with mild to moderate aphasia typically have difficulty articulating and understanding the correct words for objects and activities as well as in structuring words they do understand into sentences. Speech and language therapy can help people with mild to moderate aphasia use their remaining language functions to their best ability and learn alternate means of expression. Family and friends can assist by developing mechanisms for interpreting and understanding the person's expressions.

See also APRAXIA; ATAXIA; SPEECH DISORDERS.

apraxia The inability to engage in learned patterns of voluntary MUSCLE activity though the capability (muscle function) is present. Apraxia, also called dyspraxia, may affect various functions and tasks that require voluntary muscle activity. Among them speaking (verbal apraxia, sometimes called apraxia of speech), clapping hands or brushing the TEETH (limb apraxia), swallowing or whistling (buccofacial apraxia), using implements such as eating utensils or hand tools (motor apraxia), and moving the eyes to follow an object (occulomotor apraxia). Verbal apraxia is the most common form of this neurologic disorder.

Verbal Apraxia in Children

Developmental verbal apraxia in children results from injury, often unidentified as to its nature and cause, to the BRAIN regions and neural pathways that produce speech. Verbal apraxia begins to show symptoms between the ages of 18 and 30 months, the age in normal development at which

a child has acquired a vocabulary of several dozen to several hundred words and can speak in simple sentences. Symptoms of verbal apraxia include

- unable to shape the lips and MOUTH to form words
- appears to hear and understand but does not verbalize in response
- verbalizes only certain sounds or words
- makes inconsistent mistakes in speech

These characteristic symptoms distinguish verbal apraxia from developmental delays in speech, in which the child's language skills evolve more slowly than normal but are otherwise typical and complete. The diagnostic path includes a comprehensive speech and language evaluation as well as an assessment for HEARING LOSS. Early recognition and diagnosis allow appropriate early intervention, which focuses on training the brain to use different language pathways. Treatment is more likely to succeed when the brain is still learning these pathways. Rerouted language pathways appear to remain as redirected, becoming the "normal" language pathways for the individual, and the person speaks and otherwise manages language skills in an age-appropriate manner. However, the ultimate success of treatment depends on the nature, location, and extent of the injury to the brain, factors the neurologist often does not know.

Verbal Apraxia in Adults

Acquired verbal apraxia in adults most commonly results as a consequence of STROKE or TRAUMATIC BRAIN INJURY (TBI). The person knows what he or she wants to say but cannot formulate the words, says the wrong words, or articulates sounds that are not words (gibberish). The person knows the right words and is aware his or her words are wrong but cannot correct them. Often the mistakes in speech are inconsistent; the person may one time speak flawlessly and the next be unable to articulate recognizable words. The person may also speak with incorrect inflection and intonation, such that the rhythm of speech does not match the words. Verbal apraxia is extremely frustrating for the person who has it.

The diagnostic path typically includes imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN to identify the area of injury as well as to determine, when unknown, the cause of the injury. Aggressive speech therapy may improve speech over time. However, severe apraxia, especially when coupled with muscle weakness, may not respond to treatment. In such circumstances the emphasis shifts to teaching the person to communicate through other means such as writing or pictures. Some people experience spontaneous recovery from acquired verbal apraxia, though neurologists do not know what causes this to happen or how it happens.

See also AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; SPEECH DISORDERS; SWALLOWING DISORDERS; VELOPHARYNGEAL INSUFFICIENCY.

ataxia The inability to coordinate voluntary fine-motor movement. Ataxia may be acquired or inherited and has varied presentations. Gait and balance disturbances (difficulty with walking) are the most common symptoms. Depending on the form of ataxia, other symptoms may include disturbances of EYE movements, sensory perception, and cognition. The diagnostic path includes diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and COMPUTED TOMOGRAPHY (CT) SCAN to rule out other causes of the symptoms. Personal health history and family medical history are important.

Acquired ataxia most commonly occurs as a result of injury to the cerebellum (the division of the BRAIN responsible for fine motor movement), SPINAL CORD, or SPINAL NERVES. It may also develop as a consequence of long-term ALCOHOLISM and MULTIPLE SCLEROSIS. These forms of ataxia tend to be persistent or slowly progressive, depending on the underlying cause. Acute (sudden onset) acquired ataxia may develop following a viral INFECTION such as CHICKENPOX and EPSTEIN-BARR VIRUS. No treatment is necessary for acute acquired ataxia, as normal movement and coordination generally return within several months.

Hereditary ataxia may occur in various inheritance patterns and tends to be slowly progressive. There are several forms of hereditary ataxia, the most common of which are ataxia telangiectasia and Friedreich ataxia. Hereditary ataxia typically begins to show symptoms in early childhood when the child begins to walk. Most people retain

the ability to walk for 10 to 15 years after symptoms begin and maintain limited independence with assisted mobility (such as a wheelchair) for another 10 years or longer.

See also AMYOTROPHIC LATERAL SCLEROSIS (ALS); CEREBRAL PALSY; COGNITIVE FUNCTION AND DYSFUNCTION; GENETIC COUNSELING; INHERITANCE PATTERN; NYSTAGMUS; PARKINSON'S DISEASE; VIRUS.

athetosis Slow, writhing, involuntary, often continuous movements of the hands and fingers and occasionally the upper extremities. Athetosis occurs as a result of damage to the basal ganglia, NERVE structures deep in the BRAIN that regulate voluntary movement. Athetosis occurs in about 5 percent of people who have CEREBRAL PALSY and also as a consequence of hepatic ENCEPHALOPATHY (damage to the structures of the brain resulting from LIVER FAILURE) or encephalopathy due to drug toxicity (including ANTIPSYCHOTIC MEDICATIONS and medications to treat PARKINSON'S DISEASE), ENCEPHALITIS (INFLAMMATION of the brain), and HUNTINGTON'S DISEASE. Athetosis often occurs in combination with CHOREA (choreoathetosis).

The diagnostic path relies on physician observation in combination with health history. Imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) sometimes show the lesion (damaged tissue) within the brain. Treatment for athetosis depends on the underlying cause and may include

- MUSCLE RELAXANT MEDICATIONS such as diazepam (Valium) and clonazepam (Klonopin)
- OCCUPATIONAL THERAPY to teach adaptive skills and improve MUSCLE control
- DEEP BRAIN STIMULATION, which alters the electrical output of the basal ganglia and related structures
- RHIZOTOMY, a surgical OPERATION in which the neurosurgeon selectively severs root fibers of the SPINAL NERVES that serve the affected areas of the body

Outcome also depends on the underlying cause. Surgery is often effective at eliminating athetosis when the cause is cerebral palsy. A combination of methods often achieves relief when other causes are responsible.

See also DYSTONIA; TIC; TOURETTE'S SYNDROME; TREMOR DISORDERS.

B

Bell's palsy Damage to the seventh cranial nerve (facial NERVE) that results in partial to complete PARALYSIS of the facial structures on the affected side. Palsy is an antiquated term for paralysis. The paralysis is usually temporary, though it may take up to six months (and occasionally longer) for nerve function to return to normal. Bell's palsy is the most common form of facial paralysis, affecting more than 40,000 Americans each year.

The facial nerve has both motor and sensory functions. It controls all of the muscles in the face, the tiny MUSCLE that moves the stapes BONE in the middle EAR, the muscles that regulate the flow of tears from the tear glands (lacrimal glands), and the muscles that regulate the flow of saliva from the SALIVARY GLANDS. The facial nerve also conveys sensory signals for taste from the tongue to the BRAIN. One facial nerve serves each side of the face. The facial nerve runs from the base of the brain through a channel (the fallopian canal) in the cranial (skull) bones to its emergence at the base of the earlobe, where it divides into numerous branches that extend across the face.

The damage that results in Bell's palsy typically occurs within the fallopian canal. Researchers suspect viral INFECTION is the primary culprit, as Bell's palsy often follows a viral infection such as INFLUENZA, MENINGITIS, and HERPES SIMPLEX. Trauma to the head that compresses the facial nerve within the fallopian canal and extended irritation such as may occur with prolonged exposure to intense wind are also circumstances that can cause Bell's palsy.

Symptoms and Diagnostic Path

The most prominent feature of Bell's palsy is facial distortion resulting from paralysis of the muscles on the affected side of the face. Rarely, symptoms may involve both sides of the face. Symptoms include

- drooping of the eyelid and corner of the MOUTH
- loss of control of the facial muscles
- numbness
- excessive tearing of the EYE
- drooling (SIALORRHEA)
- HEARING LOSS or ear PAIN
- disturbances of taste

The PARALYSIS and other symptoms of Bell's palsy strike suddenly, often mimicking those of STROKE. For this reason, immediate medical assessment is crucial. Stroke is life-threatening and urgent treatment can make the difference for optimal recovery.

The diagnostic path includes a NEUROLOGIC EXAMINATION and assessment of personal health history, particularly for any recent viral infections or circumstances that cause compression or inflammation of the facial nerve. The doctor may conduct imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI) to rule out stroke, tumor, BRAIN HEMORRHAGE, and other possible causes of the symptoms. An electromyogram (EMG) may show the extent to which the nerve damage affects the facial muscles. The doctor makes the diagnosis of Bell's palsy after ruling out other possible conditions.

Treatment Options and Outlook

Treatment for Bell's palsy targets the cause of the nerve damage when the cause persists, which may

include anti-inflammatory medications to relieve swelling or ANTIVIRAL MEDICATIONS when a VIRUS appears to be the culprit. It is important to protect the eye when the paralysis affects the muscles controlling the eyelid, as the eyelid may not blink or close. The doctor may prescribe topical ophthalmic medications and protection for the eye such as an eye shield. Other therapies are primarily supportive, such as speech and swallowing therapy. Some people benefit from MASSAGE THERAPY of the face, PHYSICAL THERAPY, and ACUPUNCTURE to relieve symptoms and maintain muscle tone and health while the damage to the facial nerve heals.

About 85 percent of people recover with minimal or no residual effects. The remainder experience improvement though may have persistent paralysis and loss of function, including hearing impairment. Rarely, Bell's palsy results in significant, permanent loss of function and feeling. In such circumstances doctors may recommend corrective surgery to restore the protective capability of the eyelid as well as function and appearance of the mouth. The symptoms of Bell's palsy may take two weeks to six months or longer to fully resolve.

Risk Factors and Preventive Measures

People who have DIABETES and women who are in the third trimester of PREGNANCY are significantly more likely to develop Bell's palsy. Bell's palsy is more common as well in people who have MULTIPLE SCLEROSIS or who are IMMUNOCOMPROMISED. Researchers do not know why these circumstances increase vulnerability to Bell's palsy. There are no known preventive measures for Bell's palsy.

See also CONJUNCTIVITIS; CRANIAL NERVES; LYME DISEASE; SKELETON; SMELL AND TASTE DISORDERS.

blood–brain barrier A protective mechanism that regulates the size of molecules that may pass from the bloodstream to the BRAIN. A layer of cells called the endothelium lines the inner channel of the body's tiniest BLOOD vessels, the capillaries. The endothelium functions somewhat like a net. In parts of the body other than the brain, the cells of the endothelium are wider apart, forming a looser net that allows NUTRIENTS, chemicals, and other substances to pass into the spaces between cells. From these spaces the substances can enter the cells that need them.

In the brain the capillary endothelium is compact, its cells forming a tight net to restrict substances from crossing into the intracellular spaces. Glial cells, cells within the brain that support neurons, also participate in the blood–brain barrier, although researchers do not fully understand the mechanisms through which they do so. In some areas of the brain the blood–brain barrier is looser, allowing substances to more easily cross (though not as easily as in the body). Among these areas are the:

- area postrema, commonly called the NAUSEA center, which allows toxins in the bloodstream to rapidly trigger the vomiting REFLEX
- pineal region, the area surrounding the PINEAL GLAND
- pituitary region, the area surrounding the PITUITARY GLAND

The blood–brain barrier permits the brain to maintain balances of neurotransmitters, GLUCOSE, electrolytes, fluid, and other substances that differ from those of the body and are essential for proper brain function. The blood–brain barrier also prevents many PATHOGENS (notably BACTERIA and viruses) from entering the brain, helping reduce the likelihood of INFECTION. Many drugs are unable to cross the blood–brain barrier, though those that can include barbiturates. The body must metabolize drugs that cannot cross the blood–brain barrier, such as ANTIBIOTIC MEDICATIONS to treat infection and levodopa (a precursor of DOPAMINE taken to treat PARKINSON'S DISEASE), into substances small enough to cross the capillary endothelium to enter the brain. Thus, though it is primarily protective, the blood–brain barrier sometimes impedes therapeutic efforts. Conditions such as HYPERTENSION (high BLOOD PRESSURE, which can cause microscopic ruptures in the capillaries), STROKE, and penetrating trauma to the brain can disrupt the blood–brain barrier by allowing blood to come in direct contact with brain tissues.

See also BARBITURATES; CEREBROSPINAL FLUID; CREUTZFELDT-JAKOB DISEASE(CJD); NEURON; NEUROTRANSMITTER; PATHOGEN; VIRUS.

brain The structural and functional hub of the NERVOUS SYSTEM. The brain regulates the body's functions, voluntary and involuntary. The adult brain is a mass of soft, spongy tissue that weighs about three pounds. It receives 20 percent of the body's BLOOD flow and consumes 20 percent of the body's oxygen supply. The brain and the SPINAL CORD collectively make up the CENTRAL NERVOUS SYSTEM.

The brain resides within the enclosure of the cranium (skull). The cranium's fused bones limit the portals of direct access to the brain. The largest such portal is the foramen magnum, the opening in the occipital bones through which the spinal cord passes. Other smaller passages provide pathways for the CRANIAL NERVES, which terminate in the structures of the brainstem and the underside of the brain. Three layers of membranes, the MENINGES, wrap around the brain for further physical protection. CEREBROSPINAL FLUID circulates between the meninges, cushioning the brain as well as maintaining its biochemical balance. The BLOOD–BRAIN BARRIER, a specialized layer of cells lining the blood vessels that serve the brain, adds a final level of security by limiting the substances that can pass between the blood and the brain.

The Brain's Structure

Neurons (NERVE cells) and glial cells (support cells) form the tissue of the brain. Neurons transmit electrical impulses (nerve signals). Glial cells (also called neuroglia) make myelin, a fatty protein coating that nourishes and insulates neurons. Though the brain contains its full complement of neurons by about age three, glial cells grow and divide throughout life. Though neurons do not grow or divide, they do continue to form new connections (synapses or synaptic circuits) throughout life by extending and branching their axons, the fibers that carry nerve impulses from the NEURON to a synapse (a microscopic channel that separates one neuron from another).

Areas of the brain that contain high concentrations of neuron bodies, such as the cerebral cortex and the basal ganglia, are the gray matter, so-named because these areas are dark in color. Areas of the brain such as the inner cerebrum and the brainstem that are primarily concentrations of axons, the pathways by which neurons communicate, are the white matter. Myelin, which encases and insulates the axons to contain the electrical impulses they transmit, gives the axons their white appearance. The fully developed adult brain contains about 100 billion neurons and up to 50 times as many glial cells.

The brain's three main structural components are the forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon). Each of these divisions has further structural as well as functional subdivisions, making the brain the most complex organ of the body. For the most part the brain is a paired organ, with its two halves, the right hemisphere and the left hemisphere, roughly symmetrical in physical structure though not in function. A connecting bridge of neuronal tissue, the corpus callosum, allows the hemispheres to communicate with each other.

Within the structure of the brain are four connected spaces, called ventricles, that produce and contain cerebrospinal fluid. The lateral ventricles, also called the first and second ventricles, are the largest and contact the frontal, temporal, and occipital lobes. The third ventricle is a small space that joins with the lateral ventricles along the midline of the brain and the fourth ventricle, also small, is at the back of the brainstem and joins with the subarachnoid mater (the middle of the meninges).

The Forebrain

The forebrain is the largest of the brain's structural divisions, making up about 85 percent of the brain's mass and weight. Its composition is primarily gray matter—neuron bodies. The forebrain's subdivisions are the telencephalon and the diencephalon. The first cranial nerve, the olfactory nerve, arises from the telencephalon. The second cranial nerve, the OPTIC NERVE, originates in the diencephalon. The forebrain also contains the lateral ventricles and the third ventricle.

The telencephalon, which makes up the bulk of the forebrain, contains the:

- cerebral cortex, also called the cerebrum, which handles all of the body's functions related to conscious activity, from thought and behavior to movement and balance

- basal ganglia, collections of nerve fibers that direct motor functions related to complex movement, including the coordination of muscles and speed with which movements take place; among the basal ganglia are the caudate nucleus, putamen (corpus striatum), globus pallidus, and subthalamic nucleus
- amygdala, a pair of almond-shaped collections of neurons (nuclei) in the temporal lobes with functions related to emotion and the storage of new memories
- hippocampus, a collection of neurons in each temporal lobe with functions related to memory (especially storage and retrieval of long-term memories) and learning

The cerebral cortex features a complex structure of folds (gyri) and fissures (sulci). Each cerebral hemisphere contains four lobes—frontal, parietal, temporal, and occipital—that conduct the brain's cognitive, emotional, behavioral, analytical, interpretive, sensory, and motor activities. Though there is some overlap among the lobes in the kinds of information they process and the ways they process it, each lobe has specific functions. As well, the corresponding lobes of each hemisphere have complementary functions. The lobes of the left hemisphere handle more of the tasks and activities of logic, sequence, order, analysis, and verbal communication. The lobes of the right hemisphere handle more of the tasks and activities of emotion, imagination, intuition, and nonverbal communication.

The primary structures of the diencephalon are the:

- HYPOTHALAMUS, a mix of endocrine and nerve tissues that integrates many of the neurologic

LOBES OF THE CEREBRAL CORTEX

Lobe	Location	Key Functions
frontal	forward part of the forebrain, in front of the parietal lobes and above the temporal lobes central sulcus separates frontal from parietal lobes lateral sulcus separates frontal from temporal lobes	fine motor movement mood personality planning judgment problem solving verbal expression (Broca's area)
parietal	behind the frontal lobes and above the occipital lobes central sulcus separates parietal from frontal lobes parieto-occipital sulcus separates parietal and occipital lobes	sensory input (taste, touch, PROPRIOCEPTION) spatial relationships sensory integration reading written expression calculation
temporal	beneath and behind the frontal lobes lateral sulcus separates temporal from frontal lobes	sensory input (hearing) listening (auditory portion of speech) memory processing of complex images such as faces integration with hippocampus language processing (Wernicke's area)
occipital	behind the temporal lobes and below the parietal lobes parieto-occipital sulcus separates occipital from parietal lobes	sensory input (vision) visual processing (primary visual cortex)

and HORMONE functions of basic survival (such as body temperature regulation)

- thalamus, a small structure that filters and sorts (modulates) sensory impulses that enter and the motor impulses that leave the brain

The diencephalon incorporates the olfactory and optic tracts (origins and pathways of the first and second cranial nerves, respectively). Also within the diencephalon are the PITUITARY GLAND and PINEAL GLAND.

The Midbrain

The midbrain, also called the brainstem, is the point of origin for the third cranial nerve (oculomotor nerve) and the fourth cranial nerve (trochlear nerve). It is the neuronal bridge that joins the forebrain, hindbrain, and spinal cord. The midbrain controls primitive survival functions such as BREATHING and heartbeat. It also contains a cluster of cells called the substantia nigra which secrete DOPAMINE, a NEUROTRANSMITTER essential for movement. The death of cells in the substantia nigra causes PARKINSON'S DISEASE.

The Hindbrain

The hindbrain is beneath and to the back of the forebrain. Its two substructures are the metencephalon and the myelencephalon, which control numerous bodily functions essential for survival. The fourth ventricles are also located within the hindbrain.

The metencephalon is the point of origin for the fifth (trigeminal), sixth (abducens), seventh (facial), and eighth (vestibulocochlear) cranial nerves. The metencephalon contains the:

- cerebellum, which directs and coordinated voluntary MUSCLE function; it receives sensory input from the vestibular structures of the inner EAR (balance) and from peripheral proprioceptors (specialized sensory nerve endings in the limbs) that report the body's spatial orientation within its environment
- pons, which connects the medulla oblongata and the cerebellum with the cerebrum and from which the fifth (trigeminal), sixth (abducens), seventh (facial), and cochlear segment of the eighth (vestibulocochlear) cranial nerves originate

The myelencephalon contains the medulla oblongata, which connects the brainstem and the spinal cord. The ninth (glossopharyngeal), tenth (vagus), eleventh (spinal accessory), and twelfth (hypoglossal) cranial nerves arise from the medulla oblongata. The fourth ventricle is within the medulla oblongata. The medulla oblongata regulates BLOOD PRESSURE, HEART RATE, RESPIRATORY RATE, digestion, and elimination (URINATION and defecation), as well as reflexive actions such as sneezing and coughing.

Neuron Communication in the Brain

Brain neurons communicate with one another through electrical impulses and biochemical facilitators called neurotransmitters. Neurotransmitters conduct or block the impulse's travel across a synapse. Each brain neuron has up to 10,000 synapses, which make up its neuronal pathways; the brain overall has 50 to 200 trillion synapses. The brain sends and receives nerve impulses contralaterally—that is, the brain's right hemisphere handles functions dealing with the left side of the body and its left hemisphere handles functions dealing with the right side of the body. The brain receives sensory nerve signals from the body, which its various regions and areas process and assimilate. The brain sends motor nerve signals to the body in response.

Recent research suggests the brain appears to continually adapt and adjust its neuronal, or synaptic, pathways by extending and branching existing axons and shutting down axon branches it no longer uses. This process of continual pruning seems aimed at keeping the brain's neuronal communications streamlined and efficient and perhaps also at compensating for diminishment that may occur through aging. Though the brain is most receptive to learning during the childhood years when the establishment of synaptic pathways is at its peak, the brain remains capable of learning for the duration of the lifespan.

Health Conditions and the Brain

The brain is vulnerable to the effects of health conditions that affect other body systems as well

as to disease and injury that affects it directly. CARDIOVASCULAR DISEASE (CVD) is perhaps the most significant general health risk for the brain. Conditions such as ATHEROSCLEROSIS, CORONARY ARTERY DISEASE (CAD), and HEART FAILURE can diminish the flow of blood to the brain. HYPERTENSION (high blood pressure) is the leading cause of STROKE; stroke, in turn, is the leading cause of irreversible brain injury. Conditions that affect the body's metabolic state and balance, such as chronic CIRRHOSIS and DIABETES, may alter the brain's biochemical balance to the extent of disrupting brain function (ENCEPHALOPATHY). Direct injury to the brain may result from INFECTION (ENCEPHALITIS), BRAIN TUMOR (including metastatic cancer), traumatic injury, and neurodegenerative diseases such as ALZHEIMER'S DISEASE and Parkinson's disease.

HEALTH CONDITIONS THAT AFFECT THE BRAIN

ALZHEIMER'S DISEASE	BRAIN HEMORRHAGE
BRAIN TUMOR	CEREBRAL PALSY
COMA	CONCUSSION
CREUTZFELDT-JAKOB DISEASE (CJD)	DEMENTIA
DOWN SYNDROME	EDWARDS SYNDROME
ENCEPHALITIS	ENCEPHALOPATHY
HUNTINGTON'S DISEASE	MENINGITIS
MULTIPLE SCLEROSIS	NEURAL TUBE DEFECTS
ORGANIC BRAIN SYNDROME	PARKINSON'S DISEASE
PATAU SYNDROME	PERSISTENT VEGETATIVE STATE
SEIZURE DISORDERS	TOURETTE'S SYNDROME
TRAUMATIC BRAIN INJURY (TBI)	TREMOR DISORDERS

For further discussion of the brain within the context of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also ARTERIOVENOUS MALFORMATION (AVM); BRAIN DEATH; CIRCLE OF WILLIS; COUGH; SCOTOMA; SNEEZE.

brain cancer See BRAIN TUMOR.

brain death The permanent cessation of BRAIN function commonly accepted as the indication that life has ended. The American Academy of Neurology has established guidelines for determining whether brain death has occurred that form the basis for the criteria health-care providers in the United States apply. However, the criteria vary among states in the United States as well as among countries. In general doctors make a declaration of brain death only when there is clear and unquestionable cause for and evidence of irreversible loss of brain function, and a series of procedures consistently support the determination that all brain function is absent and has no possibility of returning. The concept and establishment of brain death has medical, legal, ethical, moral, and for many people religious components.

The need to establish brain death arises when a person has suffered catastrophic injuries, such as in a motor vehicle accident, or a catastrophic health crisis, such as HEART ATTACK or STROKE, that deprives the brain of oxygen for an extended period. Emergency treatment may place the person on life support, with MECHANICAL VENTILATION to maintain BREATHING. Removing life support generally requires medical consensus that brain death has occurred. The declaration of brain death is also necessary to harvest organs such as the HEART for ORGAN TRANSPLANTATION. In most circumstances a person's next of kin, family members, or person designated with medical power of attorney must authorize cessation of life support even with a declaration of brain death.

CARDINAL EVIDENCE OF BRAIN DEATH

clear cause for irreversible BRAIN death
no evidence of drugs or conditions that could suppress brain function
COMA
no REFLEX response to PAIN
no brainstem reflexes
no electrical activity on ELECTROENCEPHALOGRAM (EEG)

See also END OF LIFE CONCERNS; QUALITY OF LIFE.

brain hemorrhage Significant loss of BLOOD within the cranium or the tissues of the BRAIN. Most brain hemorrhages occur suddenly and unexpectedly. Occasionally brain hemorrhage may be chronic, such as when slow bleeding takes place through a small rupture in an ANEURYSM.

Brain hemorrhage has two major consequences, each of which can be life-threatening: It deprives the brain of vital oxygen and it causes increased pressure within the skull. Brain hemor-

rhage may result from trauma to the brain or from the rupturing of a blood vessel (hemorrhagic STROKE), and may occur within the tissues of the brain, between the inside of the cranium (skull) and the MENINGES (membranes that enclose and protect the brain), or between the layers of the meninges. Doctors designate the kind of bleeding by its location, which also provides clues as to the cause of the bleeding. A brain hematoma is a collection of blood, though many people use the terms *hemorrhage* and *hematoma* interchangeably in referring to bleeding in the brain.

Suspected brain hemorrhage is a potentially life-threatening emergency that requires immediate medical evaluation and treatment.

Symptoms and Diagnostic Path

Symptoms of brain hemorrhage are very much the same regardless of the location of the bleeding. They include

- severe HEADACHE that may come on suddenly or come and go
- weakness or numbness (especially if only on one side of the body)
- difficulty forming words, using the right words, or understanding what others are saying
- NAUSEA and VOMITING
- irritability
- seizures
- fluctuations in consciousness and cognitive function

The diagnostic path typically begins with a NEUROLOGIC EXAMINATION and COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) of the head. These procedures can nearly always confirm the diagnosis of brain hemorrhage as well as pinpoint its location and provide information for the neurologist to assess the severity of the bleeding and potential extent of damage. Because the standard of treatment for stroke that results from a blood clot in a blood vessel is thrombolytic medications to dissolve the clot, doctors conduct these procedures with urgency so they can initiate the appropriate treatment.

Treatment Options and Outlook

Rapid treatment is essential to stop the bleeding and relieve pressure within the brain. In many situations such treatment is emergency surgery to repair the bleeding blood vessels and drain the collected blood. The risk of dying from intracerebral hemorrhage (hemorrhagic stroke) is particularly high because the bleeding is often extensive and directly damages vital areas of the brain. The extent of residual damage after successful treatment depends on many factors and may not be

KINDS OF BRAIN HEMORRHAGE

Brain Hemorrhage	Location	Likely Causes or Contributing Factors
epidural	between the cranium and the dura mater (above the MENINGES)	blunt trauma to the head bleeding disorders
subdural	between the dura mater and the arachnoid mater (the outermost and middle meninges)	blunt trauma to the head
subarachnoid	between the arachnoid mater and the pia mater (the middle and innermost meninges)	ruptured ANEURYSM blunt trauma to the head
intracerebral	within the tissues of the BRAIN	HYPERTENSION ATHEROSCLEROSIS ruptured aneurysm ruptured vascular malformation

apparent for weeks to months after the bleeding. Some people have significant permanent consequences such as PARALYSIS, SEIZURE DISORDERS, and cognitive dysfunction. Many people who recover have minimal permanent consequences, particularly when diagnosis and treatment are immediate. PHYSICAL THERAPY, OCCUPATIONAL THERAPY, and speech therapy help restore maximum function.

Risk Factors and Preventive Measures

Trauma to the head, such as may occur in MOTOR VEHICLE ACCIDENTS or falls, is the most common cause of brain hemorrhage. Proper restraints (seat belts and car seats) and helmets worn during activities such as bicycle riding and downhill skiing, help reduce the risk for head injury. Young children and elderly adults are at highest risk for head injury due to falls. HYPERTENSION (high BLOOD PRESSURE) is the most significant preventable risk factor for intracerebral hemorrhage (bleeding within the tissues of the brain). Lifestyle factors such as cigarette smoking, which causes changes in the structure of the walls of the arteries, and lack of regular physical activity can exacerbate the effects of hypertension. People who take anticoagulant medications ("blood thinners") or who consume excessive amounts of ALCOHOL have increased risk for brain hemorrhage because these substances slow the blood's ability to clot. People who have MARFAN SYNDROME also have increased risk for brain hemorrhage as this congenital disorder causes abnormalities in the blood vessel structures.

See also COGNITIVE FUNCTION AND DYSFUNCTION; CONCUSSION; TRAUMATIC BRAIN INJURY (TBI).

brain tumor An abnormal growth that arises within the tissues of the BRAIN. Brain tumors may be noncancerous or cancerous, and cancerous brain tumors may be primary (originate in the brain) or metastatic (spread to the brain from cancer that originates elsewhere in the body). About 75 percent of cancerous brain tumors are metastatic. Primary brain cancer very seldom spreads beyond the CENTRAL NERVOUS SYSTEM (brain and SPINAL CORD). In general noncancerous brain tumors are easier to treat than primary cancerous brain tumors because they tend to remain contained.

However, the tumor's size and location are often the more relevant factors in determining treatment options and prognosis (prospects for recovery). Because the cranium, which houses the brain, is a closed space, any extra mass within it puts pressure on the tissues of the brain that can cause serious damage or death. Though all of the brain is important, some areas are vital to sustain the functions of life. A tumor growing in such an area, such as the brainstem, may become life-threatening more quickly than a tumor growing elsewhere in the brain. As well, some areas of the brain, again such as the brainstem, are inoperable—that is, a neurosurgeon cannot get to the tumor to remove it. Neurologists grade (classify) brain tumors according to their cells of origin, size, likelihood to grow in size, and likelihood to infiltrate (spread into) the tissues and supportive structures of the brain. Many brain tumors contain a combination of cell types.

TYPES OF BRAIN TUMORS

astrocytoma	chordoma
craniopharyngioma	dermoid cyst
ependymoma	epidermoid cyst
ganglioglioma	ganglioneuroma
glioblastoma	glioblastoma multiforme (GBM)
glioma	hemangioblastoma
medulloblastoma (MDL)	meningioma
neuroglioma	oligodendroglioma
pineal germinoma	pituitary ADENOMA
primary malignant lymphoma	primitive neuroectodermal tumor (PNET)

Symptoms and Diagnostic Path

The symptoms of a brain tumor depend on the tumor's location and the parts of the brain the tumor's presence affects. Though HEADACHE can be among the symptoms of brain tumor, most headaches, even those that are severe, do *not* indicate a brain tumor. Disturbances of balance, motor control (movement and coordination), special senses (sight, smell, taste, and hearing), cognitive function, memory, and emotions are common general symptoms of brain tumors. Brain tumors may also cause seizures, NAUSEA and VOMITING, and weakness or PARALYSIS on one side of the body.

The diagnostic path begins with a PERSONAL HEALTH HISTORY and NEUROLOGIC EXAMINATION, with

BRAIN TUMOR SYMPTOMS AND SIGNS

Tumor Location	Common Symptoms and Signs
cerebrum—frontal lobe	erratic behavior emotional outbursts cognitive dysfunction memory dysfunction altered sense of smell vision impairment hemiplegia or hemiparesis (PARALYSIS or weakness on one side of the body) awkward, uncoordinated movement seizures
cerebrum—occipital lobe	loss of vision in the upper half or the lower half of the field of vision seizures
cerebrum—parietal lobe	difficulty with language and speech loss of the ability to write seizures loss of PROPRIOCEPTION (spatial orientation)
cerebrum—temporal lobe	seizures disturbances of language processing and articulation
eighth cranial NERVE (vestibulocochlear nerve)	tinnitus (ringing in the ears) HEARING LOSS
midline (center of the ventral surface of the BRAIN)	persistent HEADACHE NAUSEA NYSTAGMUS vision disturbances erratic behavior or personality changes
cerebellum	awkward, staggering gait swaying when standing lack of coordination
brainstem	irritability inability to concentrate headache that is especially severe upon waking disturbances of vision and EYE function nausea and vomiting MUSCLE weakness

imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and COMPUTED TOMOGRAPHY (CT) SCAN to examine the brain's structure. Most tumors are detectable with these procedures. However, the neurosurgeon must take a sample of the tumor's cells (biopsy) to determine the type of tumor and whether it is cancerous or noncancerous. When the tumor is near the surface of the brain, the neurosurgeon can usually reach it via craniotomy (drilling or cutting a small hole through the cra-

nium). Deeper tumors may require guided stereotactic techniques in which the neurosurgeon uses an imaging procedure such as MRI to guide the insertion of a biopsy instrument to the tumor with minimal disturbance of other brain tissue. Laboratory examination of the tumor's cells combined with the visual images of the CT scan or MRI help the neurosurgeon identify and grade the tumor.

Treatment Options and Outlook

The tumor's type, grade, and location determine the appropriate treatment options. Whenever possible, surgery to remove a primary tumor (or as much of it as possible) is the preferred treatment. However, tumors that deeply infiltrate brain tissue, are very large, intertwine with BLOOD vessels, or are located in vital areas may be inoperable. As well, surgery is generally not a viable option for metastatic brain tumors. RADIATION THERAPY can kill tumor cells to shrink or eradicate the tumor. Most often, treatment combines surgery and radiation therapy. Outcomes are most promising when treatment can remove 90 percent or more of the tumor.

CHEMOTHERAPY is not generally an effective treatment for primary brain tumors because it has no effect on noncancerous tumors and because primary brain cancer typically remains contained within the brain, making it unnecessary to expose the entire body to the effects of chemotherapy. Chemotherapy may be the treatment of choice for metastatic brain cancer, however, and for certain brain cancers in very young children. For people who have brain tumors beyond the reach of current treatment options, neurologists and oncologists may recommend clinical trials that are investigating new treatments. It is important to fully understand both the risks and the potential benefits of investigational treatments before agreeing to participate in a clinical trial. Among the most promising investigational treatments are medications that specifically target certain kinds of cells such as cancer cells.

Metastatic brain cancer is very difficult to treat because the cancer is generally widespread throughout the body by the time it appears in the brain. Treatment must target the original cancer as well as the metastatic brain tumor. Chemotherapy and radiation therapy are sometimes effective in achieving REMISSION of cancers that have metastasized to the brain, though in general the outlook is not favorable for metastatic brain cancer.

Risk Factors and Preventive Measures

Neurologists do not know what causes primary brain tumors to develop. There is evidence that exposure to certain toxic chemicals, notably vinyl chloride, increases the risk for primary brain cancer. However, the correlations are not as yet conclusive. Primary brain tumors, cancerous and noncancerous, occur in people of all ages and about equally in men and women. Early diagnosis allows the widest range of treatment options, and early treatment offers the best opportunity for a positive outcome. There are no known measures to prevent brain tumors. However, lifestyle measures such as nutritious EATING HABITS, daily physical exercise, maintaining healthy weight, and not smoking all help support the body's natural IMMUNE SYSTEM efforts to resist disease and maintain the body in optimal health.

See also ACOUSTIC NEUROMA; BRAIN HEMORRHAGE; CANCER TREATMENT OPTIONS AND DECISIONS; COGNITIVE FUNCTION AND DYSFUNCTION; CONCUSSION; END OF LIFE CONCERNS; MEMORY AND MEMORY IMPAIRMENT; METASTASIS; MULTIPLE ENDOCRINE NEOPLASIA (MEN); NEUROFIBROMATOSIS; RETINOBLASTOMA; SURGERY BENEFIT AND RISK ASSESSMENT; TRAUMATIC BRAIN INJURY (TBI).

C

central nervous system The collective structures of the BRAIN and SPINAL CORD, exclusive of the CRANIAL NERVES and SPINAL NERVES (the cranial nerves and the spinal nerves, along with their branches, make up the PERIPHERAL NERVOUS SYSTEM). The central nervous system functions as the master control center for the body, maintaining processes to support basic survival as well as conducting complex voluntary and conscious activities. The cranium (skull) and spinal column (vertebrae) enclose and protect the central nervous system.

For further discussion of the central nervous system within the context of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also COMA; CONSCIOUSNESS; SKELETON; UNCONSCIOUSNESS.

cerebral palsy Disturbances of motor movement resulting from damage to the structures of the BRAIN responsible for movement, notably the basal ganglia. About 500,000 Americans, children and adults, have cerebral palsy. Cerebral palsy is permanent though nonprogressive (does not worsen over time). Though cerebral palsy often is congenital (present at birth) and may result from GENE MUTATION, it is not hereditary (passed from parents to child).

Neurologists believe about 90 percent of the damage that results in cerebral palsy occurs in PREGNANCY during the development of the NERVOUS SYSTEM, sometimes long before birth. Known causes of such damage include INFECTION, such as RUBELLA (German MEASLES) and TOXOPLASMOSIS, in the mother during pregnancy and interruptions of BLOOD flow to the developing fetus. These events may disrupt critical stages of brain development. The most vulnerable times are 3 to 20 gestational weeks, 26 to 34 gestational weeks, and 36 to 40 gestational weeks.

About 10 percent of cerebral palsy occurs as a result of injuries that occur during or after birth that deprive the brain of oxygen (HYPOXIA). Other known causes of cerebral palsy acquired in the early postnatal period include untreated NEONATAL JAUNDICE (JAUNDICE of the newborn), Rh factor BLOOD TYPE incompatibility, and head injury such as may occur in MOTOR VEHICLE ACCIDENTS or falls. Most often the causes of cerebral palsy in an individual remain uncertain and likely represent a combination of circumstances (multiple factors).

Cerebral palsy has widely variable presentations. These presentations help determine the stage of development—prenatal, perinatal, or postnatal—in which the damage to the brain occurs. Other conditions that often accompany cerebral palsy include HEARING LOSS, VISION IMPAIRMENT, developmental disorders, LEARNING DISORDERS, intellectual impairment, and SEIZURE DISORDERS. These conditions reflect damage to other structures of the brain that may have occurred as a result of exposure to the same event or circumstance responsible for the cerebral palsy (especially hypoxia). Doctors classify the forms of cerebral palsy according to the pattern of symptoms present. The four general classifications currently in use are spastic, athetoid (dyskinetic), ataxic, and mixed.

Spastic cerebral palsy Spastic cerebral palsy affects about 70 percent of those who have cerebral palsy and is the "classic" form first documented by English physician William Little in the mid-1800s. In spastic cerebral palsy the affected muscles are in a state of continuous contraction, causing them to feel and appear stiff. Spasticity affects motor movement and balance. Over time

the spastic muscles tend to remain fixed in their positions (contractures) as the contracted MUSCLE fibers eventually shorten. There are four forms of spastic cerebral palsy that affect the body in different ways:

- Spastic diplegia affects both arms and both legs, though it affects the legs more severely. The legs of people who have spastic diplegic cerebral palsy often turn in at the knees and cross with walking, causing a characteristic, awkward "scissors gait." Balance and sustained movement may be difficult. Severe leg involvement may result in the inability to walk. When arm involvement is moderate to severe, the person may need assistance to eat, bathe, dress, and carry out many of the functions of daily living.
- Spastic hemiplegia (also called spastic hemiparesis) affects the arm, trunk, and leg on one side of the body. Balance is generally better than with spastic diplegia because one side of the body functions normally, though gait is awkward. Spastic hemiplegia may also affect one side of the face, sometimes resulting in speech, eating, and swallowing difficulties. Some people who have spastic hemiplegic cerebral palsy experience tremors (uncontrollable shaking) on the affected side of the body.
- Spastic paraplegia (also called spastic paraparesis) affects only the legs. As with spastic diplegia, movement when walking may be awkward. Balance is generally better, though, because the arms and upper body function normally and can to some extend offset the dysfunctions of the lower body.
- Spastic quadriplegia (also called spastic quadriparesis) affects the entire body—face, arms, trunk, legs—with equal severity. People who have mild spastic quadriplegic cerebral palsy may function relatively normally, though people who have moderate to severe damage may be relatively immobilized and dependent on others for care.

Athetoid cerebral palsy Athetoid, or dyskinetic, cerebral palsy causes persistent, involuntary movements that are slow, rhythmic, and writhing. About 15 percent of people who have cerebral palsy have this form, which most commonly affects the arms and legs though also can involve the face. Facial involvement typically results in speech, eating, and swallowing difficulties. The movements generally subside during sleep and often intensify during emotional experiences.

Ataxic cerebral palsy Ataxic cerebral palsy is the least common form of cerebral palsy, affecting only about 5 percent of people who have cerebral palsy. Ataxic cerebral palsy affects a person's balance and coordination, causing the person to adopt a wide stance and gait. In this form of cerebral palsy muscle tone may be normal, increased, or decreased. Tasks that require rapid or prolonged movements are often the most difficult. People who have ataxic cerebral palsy may also have intention tremors, in which their arms or legs shake uncontrollably with purposeful movement such as taking a step or reaching for an object.

Mixed cerebral palsy About 10 percent of people who have cerebral palsy have a mix of the standard forms. The most common mixed form is spastic and athetoid, in which the person has both stiff, contracted muscles and involuntary, writhing movement. Mixed forms of cerebral palsy also range from mild to severe, though are more likely to interfere with mobility and independence at less severe levels because of the multiple effects.

Symptoms and Diagnostic Path

The symptoms of cerebral palsy generally do not become apparent until an infant is 2 months to 2 years old. Neurologists have identified hand preference before age 12 months as one of the first indications of spastic hemiplegic cerebral palsy; in the course of normal development a child does not acquire hand preference until older than 12 months. Infants who have cerebral palsy may reach developmental markers, such as sitting unassisted or rolling over, more slowly than normal. Some have obvious hypertonicity (tense muscles) or hypotonicity (flaccid muscles).

The pediatrician closely monitors a child at risk for cerebral palsy, regularly assessing motor skills, reflexes, and other dimensions of growth and development. Common at-risk factors include low birth weight, preterm (premature) delivery, seizure disorders, severe neonatal jaundice, Rh incompatibility, and a history of difficulties during

pregnancy. The doctor may conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN and MAGNETIC RESONANCE IMAGING (MRI) to visualize the structures of the brain. An ELECTROENCEPHALOGRAM (EEG) helps identify electrical irregularities in the brain that may identify structural abnormalities. Though none of these tests conclusively diagnoses cerebral palsy, the tests help rule out other possible causes of symptoms.

As the child grows older the symptoms of cerebral palsy often become unmistakable. Among them are

- spasticity and contractures of the limbs
- inability to crawl or walk
- vision impairment
- hearing loss
- swallowing and speech difficulties
- SIALORRHEA (drooling)
- URINARY INCONTINENCE

The severity of symptoms does not worsen, though symptoms may change over time. With some forms of cerebral palsy, notably spastic hemiplegic, symptoms may change from day to day. Spasticity may develop into contractures. However, the person's overall neuromuscular status remains unchanged. The doctor may conduct repeated NEUROLOGIC EXAMINATION and diagnostic procedures to monitor any changes in symptoms, though generally can make a firm diagnosis when the child is age three to five years.

Treatment Options and Outlook

Cerebral palsy is irreversible. Treatment targets relieving symptoms and may include medications to relieve spasticity (such as baclofen), tremors, sialorrhea, and muscle tenseness. Many people take combinations of medications tailored to their specific needs and symptoms. People who have severe spastic cerebral palsy may benefit from injections of medication into the fluid around the SPINAL CORD, which allows higher concentrations of the medication to reach the NERVE cells than the person could otherwise tolerate.

PHYSICAL THERAPY can specifically target particular muscle groups and developmental delays, and

KNOWN RISK FACTORS FOR CEREBRAL PALSY

Risk Factor	Preventive Measures
maternal RUBELLA (viral INFECTION)	rubella VACCINE before PREGNANCY
maternal TOXOPLASMOSIS (protozoan infection)	avoid contact with cat feces (such as when cleaning a litter box or working in an outdoor garden) thoroughly cook pork and lamb
preterm delivery low birth weight	appropriate and consistent PRENATAL CARE appropriate nutrition diligent management of DIABETES avoid smoking avoid drinking ALCOHOL
Rh incompatibility	Rh screening before pregnancy Rh serum to mother after birth of Rh-incompatible child to protect future children
NEONATAL JAUNDICE	PHOTOTHERAPY
head injury	methods to reduce risks for falling appropriate infant restraints in motor vehicles

is especially effective when children who have cerebral palsy are young. Parents and physical therapists work together with stretching exercises to keep muscles from contracting and activities that improve coordination and balance. Speech and swallowing therapy teaches methods for gaining optimal muscle control. Physical therapy is often a long-term, even lifelong, process with specific methods for the stages of development a child goes through during the process of growing up. Continued physical therapy often is helpful for adults who have cerebral palsy, helping to keep them as independent as possible.

Surgical approaches include THALAMOTOMY (targeted ablation, or destruction) of cells in the thalamus, a brainstem structure that helps regulate voluntary movement, operations to lengthen contracted muscles, and RHIZOTOMY (selectively cutting segments of spinal nerve roots to block nerve signals to reduce spasticity). Many people who have cerebral palsy are able to live fairly independently with assistive devices and mobility aids. Computers are especially valuable tools, with adaptive technology to allow a person who has extreme mobility limitations to communicate.

Risk Factors and Preventive Measures

Most often doctors do not know the exact causes of cerebral palsy, even when they can correlate the presentation to specific windows of prenatal development or to perinatal or postnatal events. Appropriate and consistent PRENATAL CARE helps a woman maintain a pregnancy that is as healthy as possible, reducing the risk not only for cerebral palsy but also for other complications and conditions that could harm the unborn child. Among the known causes of cerebral palsy, some are preventable and others are not.

See also ATAXIA; ATHETOSIS; CONTRACTURE; QUALITY OF LIFE; REFLEX; SPASM.

cerebrospinal fluid The liquid that circulates between the arachnoid mater and pia mater, the middle and inner MENINGES surrounding the BRAIN and SPINAL CORD. Its purpose is to cushion and protect these structures. Specialized cells that line the choroid plexuses (ventricular structures within the brain) produce cerebrospinal fluid at a rate of about 500 milliliters (mL) every 24 hours, though the amount of cerebrospinal fluid in circulation is only 150 mL. The vascular arachnoid mater absorbs cerebrospinal fluid into the BLOOD circulation. Cerebrospinal fluid is 99 percent water that contains electrolytes, GLUCOSE (sugar), and proteins. The composition, color, and pressure of cerebrospinal fluid are important diagnostic characteristics, which a neurologist may assess using LUMBAR PUNCTURE. In health cerebrospinal fluid is sterile so the presence of BACTERIA or another PATHOGEN is diagnostic of INFECTION.

CEREBROSPINAL FLUID

color	clear
volume	150 milliliters
pressure	100 to 200 millimeters of water
white blood cells	> 5 per cubic millimeter
red blood cells	none
GLUCOSE	60 to 80 milligrams per deciliter (mg/dL)
protein	20 to 45 mg/dL
sodium	138 milliequivalents per liter (mEq/L)
chloride	119 mEq/L
potassium	2.8 mEq/L

For further discussion of cerebrospinal fluid within the context of the structures and functions of the NERVOUS SYSTEM, please see the overview section "The Nervous System."

See also BRAIN HEMORRHAGE; BRAIN TUMOR; ENCEPHALITIS; MENINGITIS; MULTIPLE SCLEROSIS; NEUROLOGIC EXAMINATION.

chorea Rapid, irregular, and involuntary movements that occur as a result of damage to structures of the BRAIN, notably the basal ganglia and subthalamic nucleus, that regulate voluntary MUSCLE function. The word *chorea* is from the Greek word for "dance." Researchers believe chorea represents damage to the mechanisms within these structures that ordinarily suppress extraneous NERVE signals to the muscles. Such damage allows the signals through, creating confused and excessive motor response. Chorea often occurs in combination with ATHETOSIS (called choreoathetosis) and is a symptom rather than a condition.

Chorea usually involves the arms and legs though may also involve the face and trunk. The movements of chorea appear randomly and seem to flow from one part of the body to the other,

though often are abrupt and exaggerated. In its mildest form chorea appears as restless fidgeting; in its most severe form (called ballism) chorea prevents mobility and actions such as holding objects. Chorea occurs in numerous neurologic conditions, including HUNTINGTON'S DISEASE (formerly called Huntington's chorea), PARKINSON'S DISEASE, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), untreated NEONATAL JAUNDICE (kernicterus), RETINITIS PIGMENTOSA, and CEREBRAL PALSY. Some research suggests autoimmune processes contribute to some forms of chorea. One form of chorea, Sydenham's chorea, results from streptococcal INFECTION that migrates to the brain after untreated or undertreated STREP THROAT.

The diagnostic path depends on whether there are known neurologic conditions or the chorea is a new symptom occurring without a known underlying neurologic cause. In the latter situation the doctor conducts generalized BLOOD tests to measure thyroid HORMONE levels, electrolyte levels, cell composition of the blood, and antibodies for streptococcus. The clinician may also conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and COMPUTED TOMOGRAPHY (CT) SCAN to assess the brain's structure. Such procedures will show tumors, STROKE, and anatomic abnormalities that could be responsible for the chorea.

Treatment may include ANTIBIOTIC MEDICATIONS when blood tests identify, or the doctor suspects, strep infection. Antiseizure medications, MUSCLE RELAXANT MEDICATIONS, and some of the ANTIPSYCHOTIC MEDICATIONS (notably haloperidol) often relieve the chorea. Forms of chorea that result from transient conditions typically improve or go away within weeks to months. Forms of chorea that result from permanent damage, such as TRAUMATIC BRAIN INJURY (TBI) or HYPOXIA (extended oxygen deprivation), or from degenerative conditions, such as Huntington's disease, do not improve and may worsen as the underlying neurologic condition progresses.

See also ANTIBODY; AUTOIMMUNE DISORDERS; DYSTONIA; RHEUMATIC HEART DISEASE; SPINAL CORD INJURY; THYROID GLAND; TIC.

cognitive function and dysfunction The abilities to think, reason, concentrate, process language, and remember are key functions of the BRAIN. Numerous metabolic and neurologic conditions affect these functions, some transiently and others permanently. Medications may also alter cognitive function, either intentionally (as with the acetylcholinesterase inhibitors to treat ALZHEIMER'S DISEASE) or as undesired side effects. Adequate cognitive function is essential for learning as well as for independent living.

The two frontal lobes of the cerebrum conduct most of the functions of cognition, with the other cerebral lobes contributing processes such as sensory input and behavioral cues. The prefrontal areas of the frontal lobes are the most active in regard to cognitive functions, performing functions related to analytic thought, judgment, and concentration. Other areas of the frontal lobes regulate motor movement necessary for language expression and speech. The temporal lobes, located beneath and somewhat behind the frontal lobes, interpret language input and recall memories. One temporal lobe also contains the speech center. The structures of the limbic system, notably the amygdala and the hippocampus, control the storage of recent memories.

Symptoms and Diagnostic Path

The symptoms of cognitive dysfunction vary according to the damaged area of the brain. Symptoms tend to appear gradually when the cause of the damage is a progressive neurologic disorder. A person in the early stages of cognitive loss may:

- become easily confused
- get lost on familiar routes
- be unable to perform tasks such as using a checkbook or reading a book
- say the wrong words
- fail to remember recent events

When the cause of cognitive dysfunction is damage to the brain that occurs as a result of TRAUMATIC BRAIN INJURY (TBI) or STROKE, the cognitive loss is generally obvious though may improve over time and with treatment. The diagnostic path begins with a comprehensive medical examination, including assessment of PERSONAL HEALTH HISTORY, and a general NEUROLOGIC EXAMINATION. The

COGNITIVE FUNCTIONS OF KEY BRAIN AREAS

Brain Area	Key Cognitive Functions	Indications of Damage
cerebrum—frontal lobes	logic analytic thought judgment concentration language formation and expression planning organization	inability to conduct tasks such as simple math or preparing meals cannot get from one place to another, such as home to the store cannot follow directions or instructions difficulty finding the right words to speak or write short, fragmented attention span inability to assess right and wrong
cerebrum—temporal lobes	language interpretation memory recall	inability to understand what others say cannot remember previously learned information
cerebrum—parietal lobes	PROPRIOCEPTION (awareness of body's location in its physical environment)	inability to write
cerebrum—occipital lobes	visual interpretation	inability to read
amygdala/hippocampus	memory storage	cannot remember recent events cannot learn new information

findings determine subsequent diagnostic procedures, which often include COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to visualize brain structure and ELECTROENCEPHALOGRAM (EEG) to evaluate the brain's electrical activity. Cognitive assessment testing measures the ability to perform analytic and computational tasks; recall information; and orient to time, place, and current events.

CONDITIONS THAT MAY AFFECT COGNITIVE FUNCTION

ALZHEIMER'S DISEASE	BRAIN HEMORRHAGE
BRAIN TUMOR	CREUTZFELDT-JAKOB DISEASE (CJD)
DEMENTIA	HUNTINGTON'S DISEASE
HYPOGLYCEMIA	medication side effects
MULTIPLE SCLEROSIS	ORGANIC BRAIN SYNDROME
PARKINSON'S DISEASE	sleep deprivation
STROKE	TRAUMATIC BRAIN INJURY (TBI)

Treatment Options and Outlook

Treatment approaches target the underlying causes of cognitive dysfunction. Stopping medications and correcting metabolic disorders that disrupt thinking or memory result in rapid turnaround of symptoms arising from these causes. Because many of the areas of the brain involved in cognition are functional rather than anatomic divisions, their locations vary somewhat among individuals. This is one of the factors that creates challenge for neurologists when assessing the extent of damage and the potential for recovery of functions when the cause of the damage is injury to the brain. In most people, recovery reaches its maximum level in about two years from the time of injury. Targeted, persistent PHYSICAL THERAPY and OCCUPATIONAL THERAPY can help the brain "reprogram" to use other areas for some cognitive functions.

When the cause of cognitive loss is a progressive neurologic disorder, treatment efforts are primarily supportive and aim to maintain independent functioning for as long as possible. Medications such as acetylcholinesterase inhibitors sometimes improve symptoms in people who have Alzheimer's disease though are less predictably effective in other degenerative disorders that affect cognitive function. Other medications may improve psychiatric stability, motor function,

and related symptoms that contribute to cognition, improving the person's overall ability to engage in cognitive activities.

Risk Factors and Preventive Measures

Brain damage resulting from stroke or TBI is the leading cause of cognitive dysfunction among adults in the United States. Preventive measures that target these events correspondingly lower the likelihood of cognitive dysfunction. For stroke such measures include appropriate treatment for HYPERTENSION (high BLOOD PRESSURE) and DIABETES, the leading causes of stroke. For TBI such measures include appropriate protective devices such as seat belts in vehicles and helmets for activities that entail risk for contact injuries to the head.

There is some evidence that the herbal supplement GINKGO BILOBA helps maintain alertness and cognitive function in people who are healthy and may improve concentration and cognition in people who have mild forms of cognitive dysfunction or memory impairment. However, neither prescription medications nor herbal products have the ability to fully restore cognitive functions lost to permanent brain damage such as occurs with Alzheimer's disease or TBI.

See also ENCEPHALOPATHY; MEMORY AND MEMORY IMPAIRMENT.

coma A sustained state of loss of CONSCIOUSNESS from which a person cannot be aroused. When in a coma a person does not respond to any external stimuli, including PAIN. REFLEX responses may or may not be present, depending on the depth of the loss of consciousness. Some comas are reversible with immediate and appropriate medical intervention. However, irreversible coma typically leads to PERSISTENT VEGETATIVE STATE or BRAIN DEATH.

COMMON CAUSES OF COMA

BRAIN HEMORRHAGE	CARDIAC ARREST
DRUG OVERDOSE	ENCEPHALITIS
excessive ALCOHOL consumption	hepatic ENCEPHALOPATHY
HYPERGLYCEMIA	hypoglycemia
STROKE	toxic exposure
TRAUMATIC BRAIN INJURY (TBI)	untreated HYPOTHYROIDISM
UREMIA	

Neurologists may use various assessment approaches, such as the Glasgow Coma Scale or the Rancho Los Amigos Scale (RLAS), to evaluate the depth of a coma and the extent of damage to the BRAIN that the coma represents.

See also ANESTHESIA; DELIRIUM; UNCONSCIOUSNESS.

concussion An injury to the BRAIN resulting from a blow to the head. The blow causes the brain to jolt against the inside of the cranium (skull), causing BLOOD vessels within the brain tissue to rupture. Often these are small blood vessels and the bleeding is comparable to that of minor bruising, though any damage within the brain may have potentially serious consequences, depending on its location. Brain tissue may also swell as a protective response to traumatic injury. Concussion is the most common head injury.

Symptoms and Diagnostic Path

The symptoms of concussion vary with the severity of the blow. The symptoms of mild to moderate concussion typically include

- HEADACHE
- dizziness
- confusion or disorientation
- vision changes or disturbances such as "seeing stars" or seeing double (DIPLOPIA)
- ringing in the ears (TINNITUS)
- brief loss of memory, especially of the incident causing the concussion

The symptoms of mild to moderate concussion typically go away in 15 minutes to several hours. Symptoms that are more extensive suggest severe concussion and typically include

- severe headache
- one pupil larger than the other
- NAUSEA and VOMITING
- drowsiness or inability to stay awake
- persistent confusion
- irritability, agitation, or emotional instability
- weakness on one side of the body

A person may have a reddened area, a bruise, or swelling at the site of impact, although often

there are no outward indications that a concussion has occurred.

Because the potential for serious BRAIN damage exists even with an apparently minor concussion, a person who experiences a blow to the head that results in loss of CONSCIOUSNESS or symptoms of concussion that last longer than 15 minutes should undergo examination by a physician.

The diagnostic path includes a basic NEUROLOGIC EXAMINATION to assess the person's level of CONSCIOUSNESS and REFLEX responses. The doctor may conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to determine whether there is active bleeding within the brain and to assess the extent of damaged tissue when the concussion is severe. The doctor may also conduct an ELECTROENCEPHALOGRAM (EEG) to assess the brain's electrical activity.

GRADING OF CONCUSSION

grade 1	brief confusion but no loss of CONSCIOUSNESS
grade 2	extended confusion and little or no memory of the event that caused the concussion but no loss of consciousness
grade 3	loss of consciousness lasting a few minutes to several hours with brief to extended confusion upon return of consciousness and no memory of the event that caused the concussion

Treatment Options and Outlook

Treatment is generally watchful waiting. The doctor may choose to hospitalize the person for close medical observation or may recommend regularly arousing the person for 24 to 48 hours to monitor the person's ability to exhibit full consciousness. Most concussions are mild and recovery is complete. However, severe or repeated concussions can lead to permanent brain damage or even death. It is important to monitor a person who has had a concussion for changes in alertness, behavior, and symptoms such as headache and to seek medical reevaluation if they occur.

Risk Factors and Preventive Measures

The most common causes of concussion are MOTOR VEHICLE ACCIDENTS, team sports (especially contact sports such as football and boxing), bicycle accidents, and shaking an infant or young child.

Never shake an infant or young child, even in play. Infants and young children are particularly vulnerable to BRAIN injury that can occurs with forceful shaking (shaken baby syndrome). The damage can cause concussion or, when severe, be permanent or fatal.

Collisions and crashes when downhill skiing, snowboarding, roller skating, inline skating, and skateboarding are also common causes of concussion. Measures to reduce the risk for concussion and other injuries include using appropriate personal protective equipment and devices, such as safety belts and helmets; following safety procedures and regulations; and proper training and technique when participating in sporting activities.

See also TRAUMA PREVENTION; TRAUMATIC BRAIN INJURY (TBI).

consciousness A state of awareness of one's external environment, typically when a person is awake and the cerebrum (the largest part of the BRAIN responsible for sensory, voluntary, and cognitive functions) is fully functional. Most researchers believe consciousness results from the interactions of physiology, chemistry, cognition, and memory. However, scientists do not fully understand how consciousness occurs. A clinical assessment of consciousness typically incorporates measures of how well a person is oriented to current events and surroundings. Altered states of consciousness range from sleep, from which a person is easily aroused, to COMA, from which a person cannot be aroused. A network of nerves in the brainstem, midbrain, and cerebral cortex, the reticular-activating system (RAS), is primarily responsible for regulating the level of consciousness.

See also COGNITIVE FUNCTION AND DYSFUNCTION; DELIRIUM; HALLUCINATION; MEMORY AND MEMORY IMPAIRMENT; PERSISTENT VEGETATIVE STATE; UNCONSCIOUSNESS.

cranial nerves The 12 paired nerves that originate within the cranium (skull). The cranial nerves convey sensory signals and control motor functions primarily for the head, neck, and face. Cranial NERVE X, also called the vagus nerve, serves the organs of the trunk as well. The cranial nerves and the SPINAL NERVES combined make up the PERIPHERAL NERVOUS SYSTEM, dividing and branching throughout the body to extend nerve fibers to all tissues.

When identifying the cranial nerves numerically, neurologists generally use Roman numerals I through XII to refer to the cranial nerves or designate them as first cranial nerve, second cranial nerve, and so forth. The numbers of the cranial nerves designate the cranial nerves in order from the front to the back of the BRAIN and brainstem. Cranial nerve IV, the trochlear nerve, is the smallest, and cranial nerve V, the trigeminal nerve, is the largest of the cranial nerves. Cranial nerve X has the most diverse and extensive functions.

Types of Cranial Nerves

Cranial nerves are sensory, motor, or mixed (convey both sensory and motor signals). Sensory nerves or nerve components are afferent; they conduct signals from the body to the brain and may be general (conveying sensory information such as temperature and PAIN) or special (conveying sensory information for sight, hearing, taste, or smell). Motor nerves or nerve components are efferent; they conduct signals from the brain to the body and may be somatic (serving striated or voluntary MUSCLE), visceral (serving the smooth muscle of internal organs), or branchial (serving the structures that arise from the embryonic gill arches, which are primarily the structures of the lower face, jaw, and THROAT). The cranial nerves cross before leaving the brain and brainstem, serving structures on the opposite side of the body.

Origins and Paths of the Cranial Nerves

Cranial nerves I and II are special sensory nerves. The first cranial nerves, the olfactory nerves, originate in the olfactory bulbs at the front of the brain, in a region sometimes called the rhinencephalon. The olfactory nerve fibers unify to become the olfactory tracts as they pass along the underside of the brain and terminate in the olfactory epithelium, a structure of hairlike extensions which respond to scent molecules that enter the NOSE. The second cranial nerves, the optic nerves, originate at the front of the brain near the olfactory bulbs. The OPTIC NERVE fibers converge into the optic tracts that terminate as they enter the retinas of the eyes.

Cranial nerves VIII, the vestibulocochlear nerves, are the third purely sensory pair of cranial nerves and arise from the brainstem near the juncture of the pons and the medulla oblongata. The vestibulocochlear nerve travels parallel to cranial nerve VII, the facial nerve, through a portion of the fallopian channel (a narrow tunnel through the cranium) as each leaves the brain. Each vestibulocochlear nerve has two branches, one that terminates within the cochlea, responsible for hearing, and one that terminates within the structures of the vestibule, responsible for balance.

Cranial nerve pairs III through VII and IX through XII originate from clusters of cells within structures of the brainstem. Cranial nerves III (oculomotor nerves), IV, VI (abducens nerves), XI (spinal accessory nerves), and XII (hypoglossal nerves) have purely motor functions. The remaining cranial nerves—V, VII, IX (glossopharyngeal), and X—have mixed sensory and motor functions.

Conditions That Can Affect the Cranial Nerves

Damage to the cranial nerves may result from trauma, INFLAMMATION, INFECTION, AUTOIMMUNE DISORDERS, and tumors. Depending on the nerve affected the consequences may be disturbances of sensory perceptions, such as altered taste or diminished smell, or disturbances of motor function, such as the facial PARALYSIS of BELL'S PALSY (damage to cranial nerve VII). HERPES ZOSTER (shingles) frequently affects cranial nerve V, causing extreme pain along the involved DERMATOME (pattern of nerves) of the face. ACOUSTIC NEUROMA is a noncancerous, slow-growing tumor affecting cranial nerve VIII that causes progressive HEARING LOSS.

For further discussion of the cranial nerves within the context of the structures and functions of the NERVOUS SYSTEM, please see the overview section "The Nervous System."

See also CENTRAL NERVOUS SYSTEM; SMELL AND TASTE DISORDERS; SPINAL CORD.

THE CRANIAL NERVES

Cranial Nerve Pair	Type	Functions
I—olfactory nerve	sensory (special)	sense of smell
II—optic nerve	sensory (special)	sense of sight
III—oculomotor nerve	motor (somatic)	muscles that move the EYE up and down and side to side muscles that adjust the LENS
	motor (visceral)	muscles that constrict the pupil
IV—trochlear nerve	motor (somatic)	muscles that move the eye in a circular motion (superior oblique)
V—trigeminal nerve	sensory (general)	general sensations of the face, surface of the head, MOUTH, surface of the eye, mucous membranes of the NOSE and THROAT, front two thirds of the tongue, and jaw muscles
	motor (somatic)	muscles of chewing
VI—abducens nerve	motor (somatic)	muscles that move the eye side to side (lateral rectus)
VII—facial nerve	sensory (general)	general sensations of the face, surface of the head, and front two thirds of the tongue
	sensory (special)	sense of taste, front two thirds of the tongue
	motor (somatic)	muscles that control facial expression
	motor (visceral)	muscles that regulate the flow of tears and saliva
VIII—vestibulocochlear nerve	sensory (special)	sense of balance (vestibular function of the inner EAR) sense of hearing (cochlear function of the inner ear)
IX—glossopharyngeal nerve	sensory (general)	general sensations of the back of the tongue, back of the throat, and surface of the eardrum
	sensory (special)	sense of taste, back part of the tongue and palate
	motor (visceral)	carotid body (arterial baroreflex sensors for BLOOD PRESSURE) muscles of the throat for swallowing and GAG REFLEX muscles of the tear glands muscles of the SALIVARY GLANDS
X—vagus nerve	sensory (general)	general sensations for the bronchial structures, gastrointestinal tract, outer ear, and throat
	sensory (special)	sense of taste from the back of the palate
	motor (visceral)	muscles of the heart's ventricles muscles of the gastrointestinal tract muscles of the bronchial structures muscles of the throat
XI—spinal accessory nerve	motor (somatic)	muscles of the neck that move the head
XII—hypoglossal nerve	motor (somatic)	muscles that move the tongue and back of the throat for swallowing and speech

Creutzfeldt-Jakob disease (CJD) A rare degenerative, and at present fatal, BRAIN condition that results from the distortion and malfunction of proteins in the brain. Protein particles called prions appear to be the responsible agents. Prions are infectious, meaning they can pass from one person to another to cause disease. CJD is a brain-wasting disease that destroys brain tissue, leaving spongelike holes throughout the brain. Doctors diagnose about 300 cases of CJD a year in the United States, though many researchers feel this is an inaccurate representation of how many people develop the condition because diagnosis can take place only by examining brain tissue at autopsy. Autopsy is not a standard procedure in the United States or in most countries.

Though known to doctors for more than a century, CJD came to international prominence in the early 1990s with the discovery that a form of prion infection in cows, bovine spongiform encephalopathy (BSE), could be transmitted to humans through consumption of meat in which the nervous tissues present in the meat contained infectious prions (infectious prions occur only in nervous tissue). Researchers designated this form as variant CJD (vCJD) to distinguish it from the classic form of CJD.

Another form of CJD is iatrogenic CJD in which an individual acquires the disease as a result of medical treatments using tissues from a cadaver donor with had undiagnosed CJD. Current methods for harvesting such tissues and substances, notably dura mater for transplantation and human growth HORMONE (hGH) extracted from cadaver PITUITARY GLAND, now include procedures to reduce the risk for INFECTION.

CJD is a difficult disease to track to its origins because the time from onset to show of symptoms can be several decades. Before BSE (also called "mad cow disease") focused attention on CJD, doctors believed the malformed proteins characteristic of CJD occurred spontaneously in individuals who perhaps had a GENETIC PREDISPOSITION for such damage or had unknown environmental exposure that set the chain of events in motion. Some forms of CJD appear to have a genetic component as they tend to run in families, and researchers have identified GENE mutations that produce the defective proteins.

The discovery of infectious prions has caused some researchers to suspect that these protein particles cause nearly all CJD. Researchers do not know, however, how most people would acquire infectious prions. Only about 110 people worldwide (mostly in England where BSE first surfaced) are known to have died from CJD acquired through eating BSE-contaminated beef. About 150 people worldwide are known to have died from iatrogenic CJD acquired through medical procedures. Health-care providers and suppliers of donor tissues and products now follow more stringent preparation and sterilization techniques to kill infectious prions. These measures significantly reduce, though do not eliminate, the risk of acquired CJD.

Symptoms and Diagnostic Path

Though the incubation period for CJD is typically very long (10 to 25 years), once symptoms develop the course of the disease is quite rapid. Symptoms tend to appear with dramatic suddenness and include

- erratic behavior and emotional outbursts
- memory disturbances
- DEMENTIA
- loss of motor function (jerky movements and unsteady gait)
- cognitive dysfunction

The diagnostic path includes a comprehensive PERSONAL HEALTH HISTORY to determine any family history or exposures that suggest CJD as well as imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN and MAGNETIC RESONANCE IMAGING (MRI), which can show the damage in the brain. The neurologist makes the diagnosis on the basis of clinical findings, including the progression of symptoms, after ruling out other causes. Definitive diagnosis can be made only by analysis of brain tissue after death.

Treatment Options and Outlook

All forms of CJD are, at present, progressive and fatal. Treatment is primarily palliative, aiming to improve the person's comfort and QUALITY OF LIFE to the extent possible. CJD typically results in loss

of neurologic function that leads to death within two years after symptoms appear.

Risk Factors and Preventive Measures

Because the transmission of prion infections remains uncertain, the United States and many countries in Europe have imposed strict guidelines for tissue and blood donation. Health experts disagree as to whether there is a risk for acquiring CJD through donated blood and blood products, though the risk has been well established for certain kinds of tissues and extracted substances. Many countries now have strict regulations for the raising and slaughtering of cattle, as well as testing for the presence of BSE. These regulations are constantly evolving.

See also COGNITIVE FUNCTION AND DYSFUNCTION; FOOD SAFETY.

D

deep brain stimulation A surgical procedure to treat tremors in disorders such as PARKINSON'S DISEASE and benign essential tremor. In such conditions, researchers believe the BRAIN structures responsible for fine motor movement become unable to block extraneous NERVE signals, allowing far more nerve signals to reach the muscles. The overstimulation results in the tremors. Deep brain stimulation generally becomes a viable treatment option when noninvasive measures are no longer successful in controlling tremors and the tremors are severe enough to disrupt daily living. The neurosurgeon implants a thin wire with electrodes at the tip into the thalamus or subthalamic nucleus, structures of the brainstem responsible for fine motor movement. A battery-powered pulse generator then sends electrical signals to the electrodes. The signals block the thalamus or subthalamic nucleus from sending extraneous nerve signals to the muscles, which slows or stops the tremors.

The first step of deep brain stimulation surgery is the placement of a stereotactic halo, a circular brace the neurosurgeon attaches to the person's skull with local anesthetic to numb the areas of the skull where the halo attaches. The halo holds the instruments in precise position during the OPERATION. The second step of the surgery is implanting the electrodes. After injecting a local anesthetic to numb the SKIN and periosteum covering the cranium (which are the only areas that contain nerves sensitive to PAIN), the neurosurgeon drills a tiny hole and inserts a very thin insulated wire, feeding it slowly to the thalamus or subthalamic nucleus, using MAGNETIC RESONANCE IMAGING (MRI) to visualize and guide the path of the wire.

The person remains conscious and relatively aware during this part of the surgery, so he or she can respond to the neurosurgeon's directions and report any unusual effects. The neurosurgeon typically has the person hold a small object to monitor improvement of the tremors with the electrode's placement and activation. During the third and final stage of the operation the neurosurgeon implants the pulse generator into a pocket of tissue beneath the clavicle (collarbone) under local or sometimes general ANESTHESIA and runs the other end of the insulated wire under the skin to connect at the pulse generator. The neurosurgeon uses a computer to program the pulse generator to deliver the appropriate STRENGTH and rate of electrical impulses.

The operation lasts about 90 minutes. The neurosurgeon removes the stereotactic halo when the operation is finished. Minor side effects, usually temporary, may include tingling and balance disturbances from the wire passing through the brain. Complications are rare; when they do occur they may include excessive bleeding and postoperative INFECTION. Most people return to full and regular activities within two weeks. The batteries in the pulse generator last about five years, after which the neurosurgeon replaces the pulse generator and batteries together. Deep brain stimulation typically provides long-term relief from tremors, though in degenerative conditions such as Parkinson's disease the benefit eventually diminishes as the condition progresses.

See also QUALITY OF LIFE; SURGERY BENEFIT AND RISK ASSESSMENT; TREMOR DISORDERS.

delirium A state of extreme confusion generally resulting from reversible causes. Delirium appears to result from multiple imbalances in the brain's neurotransmitters. The causes of these imbalances are generally multiple or complex, such as the

metabolic disruptions that are the hallmark of withdrawal from prolonged ALCOHOL INTOXICATION (delirium tremens). Other metabolic disturbances, such as occur with LIVER FAILURE (hepatic ENCEPHALOPATHY) or ketoacidosis of DIABETES, also cause delirium. Some people experience delirium as a reaction to general ANESTHESIA or certain medications, or as a consequence of very high FEVER. People who are elderly are more vulnerable to delirium, though delirium may occur at any age.

The presentation of delirium, which varies widely, is often difficult to distinguish from that of disorders such as DEMENTIA. A person experiencing delirium may exhibit DELUSION, HALLUCINATION, disorientation, restlessness, and inability to concentrate. The person's recent health history, including history of substance abuse or ALCOHOLISM, generally provides the determining information. BLOOD tests may show electrolyte or GLUCOSE (sugar) imbalances. The diagnostic path focuses on finding the underlying cause. Delirium nearly always resolves when the doctor identifies and treats the underlying cause.

See also COGNITIVE FUNCTION AND DYSFUNCTION; PSYCHOSIS.

dementia The loss of cognitive function resulting from changes in the structure of or damage to the BRAIN. Metabolic disturbances that create biochemical imbalances in the body, such as chronic CIRRHOSIS, may alter the brain's biochemistry as well, establishing transient dementia (dementia that goes away when the underlying imbalance returns to normal). An ADVERSE REACTION to medication or interaction among medications may also produce symptoms of dementia that typically end when the person stops taking the medication. Most often, however, dementia represents permanent loss of abilities related to thought, memory, logic, analysis, calculation, planning, and organization.

Degenerative neurologic disease ALZHEIMER'S DISEASE, PARKINSON'S DISEASE, HUNTINGTON'S DISEASE, and other progressive, degenerative conditions affecting the brain are the primary causes of dementia. These conditions cause the death of neurons in areas of the brain that conduct cognitive activities and are the most common causes of dementia.

Lewy body dementia Lewy bodies are abnormal protein deposits that form in the structures of the midbrain. Because the midbrain handles functions related to basic emotional response (such as fear and anger) and basic motor function, Lewy body dementia typically produces symptoms that appear a blend of Parkinson's disease and Alzheimer's disease. Some researchers believe the three conditions may share common origins, though the mechanisms of their relationship remain undetermined.

Vascular dementia STROKE, TRANSIENT ISCHEMIC ATTACK (TIA), BRAIN HEMORRHAGE, carotid ATHEROSCLEROSIS, and cerebral vascular disease (atherosclerosis affecting the arteries within the brain) deprive areas of the brain of the BLOOD supply they require to remain functional. Brain neurons can survive only a short time (three minutes or less) without oxygen; the body cannot replace lost neurons as it can certain other types of cells.

Traumatic brain injury Injury to the brain such as may occur in MOTOR VEHICLE ACCIDENTS may permanently damage areas of the brain. TRAUMATIC BRAIN INJURY (TBI) is the most common cause of dementia in people under age 60. Depending on the extent and location of the injury, it is sometimes possible to retrain other areas of the brain to carry out some of the lost cognitive functions.

Symptoms and Diagnostic Path

The symptoms of dementia may appear gradually or suddenly depending on the cause. They typically include

- loss of memory, which may manifest in terms of forgetfulness, failure to recognize familiar people and places, and inability to carry out familiar activities such as cooking or driving to the store
- inappropriate behavior, such as outbursts of anger
- inability to find the right words when speaking
- personality changes
- inability to make basic decisions, such as which shirt to wear or what to eat
- pronounced decline in PERSONAL HYGIENE (bathing and wearing clean clothes)

The diagnostic path begins with a comprehensive medical examination to look for common and

easily remedied causes for the symptoms. Among such causes might be undiagnosed conditions such as HYPOTHYROIDISM, DIABETES, vitamin B_{12} deficiency, neurosyphilis, and medication reactions or interactions. The doctor will also take a careful medical history, looking for evidence of recent injury or trauma or of family history of conditions such as Parkinson's disease and Alzheimer disease. The doctor may conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and COMPUTED TOMOGRAPHY (CT) SCAN to rule out BRAIN TUMOR, brain hemorrhage, or stroke. Dementia is generally a clinical diagnosis based on symptoms and on ruling out treatable causes of the symptoms.

Treatment Options and Outlook

Treatment and outlook vary with the cause of the dementia. Metabolic dementia is often transient, with normal brain function returning when treatment restores the body's metabolic balance. Dementia that results from injury to the brain or neurodegenerative conditions such as Alzheimer's disease is generally permanent. Treatment aims to improve remaining cognitive abilities through activities that use and exercise the brain, such as reading and crossword puzzles. Adaptive measures may also help, such as writing out instructions or drawing maps or pictures. Persistent, and particularly progressive, dementia may result in loss of independent function.

Risk Factors and Preventive Measures

Age is the primary risk factor for dementia. About half of people over age 85 have Alzheimer's disease, the leading cause of dementia. Lewy body dementia and vascular dementia also become significantly more common with advanced age. Appropriate medical and lifestyle management of conditions such as HYPERTENSION (high BLOOD PRESSURE), atherosclerosis, LIVER disease, and diabetes helps mitigate their health consequences.

See also COGNITIVE FUNCTION AND DYSFUNCTION; CREUTZFELDT-JAKOB DISEASE; DELIRIUM; MEMORY AND MEMORY IMPAIRMENT.

dermatome A region of the body a specific, single spinal NERVE root serves. The SPINAL NERVES convey motor signals to and sensory signals from the body. The body's dermatome pattern is fairly consistent among individuals though each person has subtle unique characteristics. Identifying the involved dermatome for chronic PAIN, MUSCLE weakness, or PARALYSIS helps the neurologist determine the region of the spine where the damage originates. This is particularly useful for therapies such as NEURAL BLOCKADE (NERVE BLOCK) and RHIZOTOMY, which are treatments for intractable pain or spasticity. The body's dermatome has the appearance of a topographic map when rendered as a visual representation.

A dermatome is also a bladed surgical instrument used to remove very thin layers of SKIN such as for skin transplantation.

See also CEREBRAL PALSY; COMPLEX REGIONAL PAIN SYNDROME; SPINAL CORD INJURY.

dyskinesia Abnormal, involuntary movements. Dyskinesia results from damage to the structures within the BRAIN responsible for motor movement and coordination, notably the basal ganglia. ATHETOSIS, CHOREA, DYSTONIA, MYOCLONUS, tics, and tremors are all forms of dyskinesia that may appear in neurologic disorders such as PARKINSON'S DISEASE, HUNTINGTON'S DISEASE, TOURETTE'S SYNDROME, RESTLESS LEGS SYNDROME, CEREBRAL PALSY, and essential benign tremor. Abnormally slow movements are bradykinetic (bradykinesia) and abnormally rapid movements are hyperkinetic (hyperkinesis). It is common for people who have neuromotor disorders to have more than one form of dyskinesia. Medications such as anticholinergics and MUSCLE relaxants can sometimes improve dyskinesia.

Tardive dyskinesia is a form of dyskinesia that develops with long-term use of DOPAMINE antagonist medications, which block dopamine from reaching dopamine receptors in the brain. Dopamine antagonists are the convention of treatment for Parkinson's disease. Many ANTIPSYCHOTIC MEDICATIONS to treat SCHIZOPHRENIA and other serious psychiatric illnesses also are dopamine antagonists. Tardive dyskinesia is often irreversible.

See also TREMOR DISORDERS.

dyslexia See LEARNING DISORDERS.

electroencephalogram (EEG) A diagnostic procedure that records the electrical activity of the BRAIN. The neurologist uses EEG to assess the brain's function. Electrodes attached to the scalp detect the brain's electrical impulses and carry the signals to the EEG machine. An amplifier converts the impulses into patterns that the machine records either in analog form (in which styluses create tracings on a slowly moving roll of paper) or digital form (in which a computer creates an electronic record).

Reasons for Doing This Test

Neurologic conditions, from BRAIN HEMORRHAGE to BRAIN TUMOR to SEIZURE DISORDERS, cause predictable and detectable deviations from the normal electrical patterns. EEG also shows the level of electrical activity in the brain of a person who is UNCONSCIOUS, in a COMA, or in a PERSISTENT VEGETATIVE STATE. The neurologist must interpret the EEG findings in context with the person's age, PERSONAL HEALTH HISTORY, medications, and other clinical findings to arrive at a diagnosis.

Preparation, Procedure, and Recovery

EEG generally requires no preparation or recovery and does not cause discomfort. To conduct the EEG, the technologist first measures the scalp to determine the sites for placing the electrodes. The sites represent a standard pattern, the most common of which is called the 10/20 system in reference to the relationships among the sites. A key of letters and numbers denote the lobe and the electrode's position. The technologist then attaches electrodes to locations on the scalp. Small dots of glue hold the electrodes in place; the glue may be difficult to remove when the EEG is over. During the EEG the person lies on a table in a quiet, darkened room while the technologist allows the EEG machine to record the electrical impulses the electrodes pick up and conduct to the machine. The technologist may use flashing or steady light to stimulate areas of the brain. A typical diagnostic EEG of the brain may take 15 to 90 minutes to complete.

The different regions of the brain generate characteristic patterns of electrical activity, measured in Hertz (Hz). EEG typically captures five types of electrical activity or brain waves:

- Alpha waves are 8 to 13 Hz, originate from the forward lobes, normally are present only when the eyes are closed, and form a moderate-amplitude symmetrical pattern.
- Beta waves are 2 to 13 Hz, originate from the back lobes, normally are present during wakefulness, and form a low-amplitude symmetrical pattern.
- Delta waves are 0 to 4 Hz, normally are present only during deep sleep, and form a high-amplitude symmetrical pattern.
- Theta waves are 4 to 8 Hz, normally are present during the transition from wakefulness to sleep, and form a moderate-amplitude erratic pattern.
- A pattern of spikes and waves is always abnormal, features erratic amplitude and cycle, and typically indicates a seizure disorder.

Risks and Complications

There are no risks or complications from EEG. There is no discomfort from attaching the electrodes or during the recording process. Sometimes removing the electrodes pulls the HAIR, and the

glue used to attach the electrodes to the scalp may be difficult to cleanse from the hair.

See also APNEA; NEUROLOGIC EXAMINATION; SLEEP DISORDERS.

encephalopathy Widespread (as opposed to localized) dysfunction of the BRAIN. Encephalopathy may be short term and temporary or result from irreversible damage to the brain such as can occur with metabolic, infectious, and degenerative diseases. Symptoms of encephalopathy include

- personality changes
- mood swings
- cognitive dysfunction
- memory impairment
- slurred speech
- disorientation
- UNCONSCIOUSNESS or COMA

The diagnostic path begins with a comprehensive medical examination, discussion of PERSONAL HEALTH HISTORY, and basic NEUROLOGIC EXAMINATION. BLOOD tests to measure electrolytes, enzymes, blood composition, GLUCOSE and INSULIN levels, and HORMONE levels can provide clues as to whether there is a condition of metabolic imbalance. The doctor may conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to visualize the structures of the brain and detect any abnormalities.

Treatment targets the underlying condition. Some forms of encephalopathy are reversible, though encephalopathy may be an end-stage circumstance in conditions such as LIVER failure or RENAL FAILURE. Encephalopathy resulting from degenerative neurologic conditions such as CREUTZFELDT-JAKOB DISEASE (CJD) is not reversible. Many people who recover from encephalopathy have no long-term residual effects. Some people may have persistent symptoms such as cognitive dysfunction or mood swings, or may develop SEIZURE DISORDERS.

CONDITIONS ASSOCIATED WITH ENCEPHALOPATHY

ALCOHOLISM	ALZHEIMER'S DISEASE
BRAIN HEMORRHAGE	BRAIN TUMOR
CIRRHOSIS	CREUTZFELDT-JAKOB DISEASE (CJD)
DRUG OVERDOSE	ENCEPHALITIS
END-STAGE RENAL DISEASE (ESRD)	Hashimoto's THYROIDITIS
HEAVY-METAL POISONING	HEMATOCHROMATOSIS
HYPERTENSION	HYPOXIA
ILLICIT DRUG USE	LIVER FAILURE
PARKINSON'S DISEASE	POLIOMYELITIS
STROKE	WILSON'S DISEASE

See also DEMENTIA; END OF LIFE CONCERNS; LIFESTYLE AND HEALTH; ORGANIC BRAIN SYNDROME.

epilepsy See SEIZURE DISORDERS.

G–H

Guillain-Barré syndrome A rare disorder in which the IMMUNE SYSTEM attacks the myelin sheaths of the PERIPHERAL NERVES, causing weakness or PARALYSIS, diminished reflexes, and loss of feeling. The loss of myelin strips the NERVE axons of insulation, inhibiting their ability to conduct electrical impulses. Doctors do not know what causes Guillain-Barré syndrome but believe it is a complication of bacterial or viral INFECTION. The most common association is with *Campylobacter jejuni*, which causes the foodborne illness CAMPYLOBACTERIOSIS. Other associations are with INFLUENZA, PNEUMONIA, GASTROENTERITIS, and some vaccinations.

Symptoms and Diagnostic Path

Symptoms typically are acute, beginning 7 to 10 days after the precipitating event (such as viral infection) and reaching peak severity within 14 days. Commonly, tingling and weakness, and sometimes PAIN, begin with the feet and move symmetrically up the body. The weakness may become paralysis, depending on the extent of demyelinization that takes place. Some people experience mild symptoms and others experience symptoms that result in complete paralysis including respiratory distress. Some people experience irregularities in HEART RATE, RESPIRATION RATE, BLOOD PRESSURE, and other autonomic functions. About half of people who develop Guillain-Barré syndrome have moderate to severe pain with movement.

The diagnostic path includes careful assessment of recent PERSONAL HEALTH HISTORY, notably for viral or bacterial infection, and procedures such as LUMBAR PUNCTURE, nerve conduction studies, and COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to rule out other causes of the symptoms. Though there is no single conclusive test for Guillain-Barré syndrome, the pattern of symptoms and findings allow the neurologist to make a clinical diagnosis.

Treatment Options and Outlook

Treatment is primarily supportive though some people improve with intravenous IMMUNOGLOBULIN, which helps restore normal immune system function, or plasmapheresis, which removes antibodies from the BLOOD. Most people require hospitalization. About 30 percent of people require temporary MECHANICAL VENTILATION until function returns to the muscles that conduct breathing.

About 85 percent of people make a complete recovery, without residual effects, in six months to a year though may need PHYSICAL THERAPY and other supportive treatment to regain MUSCLE STRENGTH and function. About 10 percent of people have residual neurologic complications such as altered sensation or weakness of the hands and feet. Very rarely, paralysis persists. Guillain-Barré syndrome is fatal in about 5 percent of people, usually in those who are older (age 65 or more) or who experience very rapid progression to complete paralysis and respiratory failure.

Risk Factors and Preventive Measures

About two thirds of people recall a viral or bacterial infection within 2 to 12 weeks of their neurologic symptoms. The most significant risk for Guillain-Barré syndrome is *C. jejuni* infection (campylobacteriosis). CYTOMEGALOVIRUS (CMV), EPSTEIN-BARR VIRUS (infectious mononucleosis), and varicella-zoster virus (CHICKENPOX) are other infections commonly associated with Guillain-Barré syndrome. There are no measures known to prevent the syndrome.

See also ANTIBODY; MONONUCLEOSIS, INFECTIOUS; MULTIPLE SCLEROSIS.

Huntington's disease An inherited, degenerative disorder of structures in the BRAIN that regulate movement, mood and personality, and cognitive function and memory. Huntington's disease follows an autosomal dominant INHERITANCE PATTERN, with each child of an affected parent having a 50 percent chance of inheriting the GENE MUTATION that allows the condition to develop. The defective gene is IT-15 on CHROMOSOME 4. It causes an alteration in a protein called the Huntington protein that has a key, though poorly understood, role in maintaining the putamen and the caudate nucleus, two structures within the basal ganglia. All people have the Huntington protein; the protein's function becomes defective when the gene that regulates it is mutated. People who have the mutation for Huntington's disease will develop the disorder, generally in midlife though occasionally the disorder manifests in late ADOLESCENCE (juvenile Huntington's disease).

Symptoms and Diagnostic Path

Early symptoms of Huntington's disease are general and may not appear related. They include

- irritability
- DEPRESSION, BIPOLAR DISORDER, or anxiety
- anger and hostility
- diminished energy
- disturbances of balance and coordination
- forgetfulness
- inability to concentrate
- delusions and hallucinations

As the disease progresses the neuromuscular symptoms become more pronounced and include DYSKINESIA (notably CHOREA and ATHETOSIS) and DYSTONIA. Cognitive dysfunction also becomes prominent, and the person may no longer recognize familiar places and people. PSYCHOSIS may also increase.

The diagnostic path includes a comprehensive medical examination, detailed exploration of PERSONAL HEALTH HISTORY and FAMILY MEDICAL PEDIGREE, and NEUROLOGIC EXAMINATION. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) may show changes in the brain characteristic of Huntington's disease though these changes are not conclusively diagnostic. The only certain diagnostic procedure is GENETIC TESTING, done from a sample of BLOOD, to determine whether the IT-15 gene is defective.

Treatment Options and Outlook

Huntington's disease is progressive and fatal, generally causing death 15 to 30 years after the onset of symptoms. Treatment aims to improve symptoms and QUALITY OF LIFE. Treatment may include ANTIPSYCHOTIC MEDICATIONS, ANTIDEPRESSANT MEDICATIONS, ANTIANXIETY MEDICATIONS, and BOTULINUM THERAPY to relieve dystonia. Therapeutic needs and effectiveness changes as the disease progresses. Emotional support through counseling and SUPPORT GROUPS is often helpful for the person who has Huntington's disease and for family members and caregivers. Most people who develop Huntington's disease can remain active and independent for 10 years or so after the onset of symptoms.

Risk Factors and Preventive Measures

The only risk for Huntington's disease is genetic. As yet researchers do not know how to prevent Huntington's disease from developing in those who carry the mutated gene. Genetic testing to detect the presence of the gene in people who have a family history of Huntington's disease but have no symptoms themselves is available; however, it is because there are no known treatments for the disorder. Though finding the gene is normal is a great relief, learning one carries the mutated gene is often a difficult challenge. Some people prefer to know so they can make appropriate plans and decisions, including family planning. Health experts strongly recommend GENETIC COUNSELING for people who have family history of Huntington's disease or symptoms that suggest Huntington's disease.

See also COGNITIVE FUNCTION AND DYSFUNCTION; DELUSION; END OF LIFE CONCERNS; HALLUCINATION; MEMORY AND MEMORY IMPAIRMENT; PARKINSON'S DISEASE.

hydrocephaly Excessive cerebrospinal fluid within the cranium (skull). Hydrocephaly, also called hydrocephalus, may develop for numerous reasons, such as congenital BRAIN defects, TRAU-

MATIC BRAIN INJURY (TBI), meningitis, subarachnoid hemmorage, and brain tumors. Untreated or uncontrolled hydrocephaly places pressure on the structures of the brain and can displace brain tissue, causing permanent damage to the brain. In an infant whose cranium has not yet fused, hydrocephaly may cause the head to enlarge as the pressure of the excessive fluid pushes the bones outward.

Hydrocephaly occurs when the brain's ventricles produce too much CEREBROSPINAL FLUID or there is an obstruction that blocks the flow of the fluid through the ventricles and spinal canal. Diagnostic prenatal ULTRASOUND often detects hydrocephaly in an unborn child. After birth or in adults, MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN can identify hydrocephaly, which most commonly occurs as a complication of INFECTION or blunt trauma (closed injury) to the brain. Symptoms are difficult to distinguish from those of the underlying condition, though may include severe HEADACHE, NAUSEA, and VOMITING.

Treatment for hydrocephaly is usually surgery to place a shunt in the brain ventricle to drain the excessive cerebrospinal fluid. The shunt is a small, rigid catheter that attaches to a one-way valve (to prevent cerebrospinal fluid from flowing back into the brain). The valve in turn attaches to a long, thin, flexible catheter that the surgeon channels beneath the SKIN to drain into the peritoneal cavity. The body then absorbs the fluid. Treatment also targets any underlying causes for the hydrocephaly. Usually the shunt is a permanent therapy, though may require periodic replacement. The risks of shunting are postoperative infection and deterioration of the shunt, valve, or catheter.

See also BIRTH DEFECTS; BRAIN TUMOR; SPINA BIFIDA.

L

learning disorders Difficulties with cognitive functions such as analytical thinking, reading, writing, speech, listening, comprehension, and memory. Learning disorders are neurologic and arise from physical disturbances in BRAIN function. Such disturbances may be due to abnormalities in brain structure that occur during fetal development, injuries to the brain that result from oxygen deprivation during PREGNANCY or CHILDBIRTH, or TRAUMATIC BRAIN INJURY (TBI) during childhood. Frequently, however, the reason for a learning disorder remains unknown. Though social factors influence the extent to which a person who has learning disorders is able to overcome challenges, such factors do not cause learning disorders.

Symptoms and Diagnostic Path

Often the first indication of a learning disorder is a gap between a child's abilities and the abilities that are normal for the child's age. Depending on the type of disorder, this gap may become apparent early in childhood or be detected when the child starts school. Symptoms may include a child's inability to

- speak in sentences by age 3
- speak clearly enough for others to understand by age 3
- tie shoes and fasten buttons by age 5
- sit still through the reading of a short story by age 5
- read and write as expected for age or grade level

Some learning disorders also involve deficits in motor skills and physical coordination. Because the rate and nature child development varies widely, diagnosing learning disorders is often challenging. The diagnostic path may incorporate numerous approaches including neurologic, vision, hearing, and speech pathology evaluations; psychologic testing; achievement testing; and classroom observation. It may be difficult to reach a clear diagnosis; test results may be inconclusive or inconsistent. In the United States, diagnostic testing and remedial or adaptive educational services are available at no cost to families for all children from birth to age 21.

Treatment Options and Outlook

Treatment is often multidisciplinary, integrating alternate learning approaches with appropriate PHYSICAL THERAPY, speech pathology, OCCUPATIONAL THERAPY, and counseling. Treatment efforts may involve the entire family. The rate and extent of progress varies widely and depends on multiple factors. Many people learn to compensate for their learning disorders to the extent that they are able to lead normal, productive lives. For some people, learning disorders present lifelong challenge.

Risk Factors and Preventive Measures

Because learning disorders result from neurologic damage, they are very seldom preventable. Appropriate PRENATAL CARE is important to provide optimal opportunity for healthy fetal development and growth. Appropriate care during childbirth and in the immediate newborn stage is especially crucial. Some learning disorders, such as dyslexia (difficulty reading), appear to run in families, leading researchers to believe genetic components may be involved.

See also APHASIA; APRAXIA; ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD); CEREBRAL PALSY; COGNITIVE FUNCTION AND DYSFUNCTION; DOWN SYNDROME;

FETAL ALCOHOL SYNDROME (FAS); HEARING LOSS; MEMORY AND MEMORY IMPAIRMENT; SPEECH DISORDERS.

lumbar puncture A diagnostic procedure, colloquially called spinal tap, in which the doctor inserts a needle between the lumbar vertebrae in the lower back to withdraw CEREBROSPINAL FLUID from the spinal canal for laboratory examination. The point of entry into the spinal canal is below the end of the SPINAL CORD, so there is no risk of the needle entering the spinal cord.

Reasons for Doing This Test

Cerebrospinal fluid may contain BACTERIA, BLOOD, or alterations of its composition that may suggest or confirm numerous conditions affecting the BRAIN and spinal cord such as INFECTION, INFLAMMATION, cancer, certain brain tumors, BRAIN HEMORRHAGE, and MULTIPLE SCLEROSIS. Lumbar puncture may also return negative results that rule out such conditions. The doctor may use therapeutic lumbar puncture to administer medications, such as baclofen as treatment for severe spasticity due to cerebral palsy or other neurologic disorders, or CHEMOTHERAPY drugs for certain cancers affecting the brain or spinal cord.

Preparation, Procedure, and Recovery

There is no advance preparation for lumbar puncture. Immediately before the procedure the doctor cleanses the area where the needle will enter the spinal canal. The person may lie on his or her side with knees drawn to chest, or sit with the head on a pillow that is resting on a table. These postures bend the spine in such a way as to open the spaces between the vertebrae. The doctor administers a local anesthetic to numb the SKIN at the insertion site. The doctor measures the pressure of the cerebrospinal fluid immediately upon the needle's entry, then allows small samples of fluid, usually about three milliliters total, to drip through the needle into collection containers. The laboratory will run different tests on each sample.

Some people experience discomfort or tingling sensations when the doctor inserts the needle into the spinal canal; occasionally the needle contacts a spinal NERVE rootlet. When finished collecting fluid samples, the doctor withdraws the needle and puts a pressure bandage over the site. Some doctors recommend lying flat in bed for three to four hours after the lumbar puncture to reduce the risk for postlumbar puncture HEADACHE, though lying flat does not always prevent this common complication. The brain's ventricles continuously replenish cerebrospinal fluid, completely replacing the full volume circulating in the brain and spinal cord three to four times a day.

The entire procedure takes about 20 minutes. Some results may be available from the laboratory within a few hours, while other results may take several days to several weeks, depending on what tests the doctor requested.

Risks and Complications

The primary risk of lumbar puncture is introducing bacteria into the cerebrospinal fluid that causes infection, which occurs rarely. Some people experience bleeding after the procedure. Headache is the most common complication, affecting about one fourth of people who have lumbar puncture. The headache may be mild to severe and typically lasts 24 to 48 hours. Unfortunately PAIN-relief medications (ANALGESIC MEDICATIONS) do not usually help the headache. Tiredness and backache are also common for a day or two after the procedure.

See also BRAIN TUMOR; NEUROLOGIC EXAMINATION.

M

memory and memory impairment The abilities to recall past events and to anticipate future events are hallmarks of the human experience and their diminishment an indication of various disorders that affect BRAIN function. Memory is the process by which the brain stores and retrieves information. Memory impairment may affect the processes of memory storage, memory retrieval, or both, and may be temporary or permanent.

Mechanisms of Memory Storage and Retrieval

The brain manages memories through multiple processes, both organic and functional, that involve numerous areas of its lobes and structures. Most researchers believe the brain stores memories in bits and fragments, which it then reassembles when recalling a specific memory. Cognitive processes (thought and analysis) and emotion significantly shape memory storage and recall, even, some experts believe, to the extent of causing memory errors and false memories. Such memory mistakes can occur when the brain blends events in the processes of storing and retrieving. Accordingly, there is much controversy among medical as well as legal professionals about the objectivity and precision of memory.

Storing memories begins with sensory or emotional NERVE impulses that travel to the brain. Different areas of the brain receive, interpret, and encode (prepare for storage) the various kinds of nerve impulses that arrive. Memory is either short-term (transient) or long-term (relatively permanent). Bridging the two is working memory, through which the brain encodes information to allow its storage in long-term memory. The extent to which a person gives attention to incoming information helps determine whether and how the information enters memory. The hippocampus, an area of the temporal lobe, is essential for forming new memories. The hippocampus also is the area of the brain responsible for emotion and emotional expression.

The mechanisms of short-term memory—information the brain retains for seconds to minutes, such as the name of the waiter taking a menu order or the amount of a purchase—appear to create only temporary shifts in neuronal connections. The information has transient (and often time-limited) value so the brain gives it transient attention. The mechanisms of long-term memory—memory of events and people from days to decades ago—create permanent changes in the neuronal pathways among cells in the regions of the brain that participate in memory storage and retrieval. Once formed, these pathways appear to remain intact and fully functional even when there is no retrieval for extended periods of the memories they connect.

Researchers categorize long-term memory as either explicit (also called declarative) or implicit (also called nondeclarative or procedural). Explicit memory requires conscious attention to recall information, such as when taking a test or telling the story of a childhood event. Explicit memory appears to involve primarily the frontal, temporal, and parietal lobes of the cerebral cortex. Implicit memory contains information the brain retrieves and acts on automatically, without conscious attention. Riding a bicycle, playing a musical instrument, driving a car, and throwing a ball are common functions of implicit memory. Implicit memory involves primarily the prefrontal cerebral cortex and the cerebellum, which coordinate voluntary MUSCLE activity, and the amygdala, a small almond-shaped structure in front of the hippocampus that governs fear and fear response.

The amygdala also appears to be where face recognition, in conjunction with emotional associations such as love or fear, takes place.

Memory retrieval requires activating, or stimulating, the neuronal pathways that connect the stored information. This involves interactions among neurotransmitters, hormones, and electrical impulses, though precisely how these interactions happen remains a mystery. Some memory retrieval occurs in response to external cues and stimuli, such as responding to questions or seeing a familiar face. Implicit memory retrieval appears activated by exposure to a circumstance, for example getting on a bicycle or behind the wheel of a car. Explicit memories are more complex. Those with strong emotional connections seem more rapidly and vividly recalled.

Causes of Memory Impairment

Everyone experiences occasional forgetfulness, most commonly with respect to recent information. Such forgetfulness may range from the names of newly introduced people to where the car keys are or the driving route to give a coworker a ride home. Many researchers believe such forgetfulness represents an incompletion in the brain's processes for establishing neuronal pathways. Only when information becomes repetitious does the brain create connections among neurons to accommodate it. The more frequently a person encounters the same information (such as a person's name), the more complete the neuronal connections among the various regions of the brain that store the information. Forgetfulness may also represent the brain's efforts to "clean house" and maintain efficiency by purging unused or extraneous information.

Memory impairment occurs when the brain cannot establish new neuronal pathways to store new memories or use existing neuronal pathways to retrieve memories already stored. A person experiencing memory impairment may be unable to remember the names of close family members or how to drive home from the store. Though memory and cognition (thought and reason) are distinct functions within the brain, neither is especially effective without the other. Correspondingly, cognitive dysfunction and memory impairment often occur together. Because researchers do not fully understand the mechanisms of memory, they do not fully understand how memory impairment occurs.

The quality of memory, particularly short-term memory, normally diminishes somewhat with advanced age (age 70 and beyond). Though forgetfulness tends to become more common as people get older, significant memory impairment is *not* an inherent dimension of aging. Much age-associated memory impairment results from conditions that occur with aging. ATHEROSCLEROSIS, in which plaque deposits accumulate in the walls of the arteries to narrow the passageways for BLOOD, is among the leading causes of impaired memory in older adults. Neurologic disorders that affect memory, such as ALZHEIMER'S DISEASE and DEMENTIA, almost exclusively occur in people over age 60.

Circumstances that can affect memory in people of any age include BRAIN TUMOR, INFECTION such as ENCEPHALITIS or MENINGITIS, systemic neurologic conditions such as MULTIPLE SCLEROSIS, and disorders that alter the body's chemical balance such as LIVER disease or untreated metabolic disorders. Memory impairment may be transitory (come and go, such as with a TRANSIENT ISCHEMIC ATTACK [TIA]), may return when treatment resolves the underlying cause (such as when the brain heals after an infection or surgery), or may be permanent (which occurs when there is tissue damage or loss in areas of the brain that perform functions of memory, such as often occurs with STROKE or TRAUMATIC BRAIN INJURY [TBI]).

CONDITIONS THAT CAN AFFECT MEMORY

ALZHEIMER'S DISEASE	ATHEROSCLEROSIS (cerebral vascular disease)
BRAIN HEMORRHAGE	CREUTZFELDT-JAKOB DISEASE (CJD)
CONCUSSION	ENCEPHALITIS
DEMENTIA	HUNTINGTON'S DISEASE
ENCEPHALOPATHY	ORGANIC BRAIN SYNDROME
MENINGITIS	SEIZURE DISORDERS
PARKINSON'S DISEASE	TRANSIENT ISCHEMIC ATTACK (TIA)
STROKE	
TRAUMATIC BRAIN INJURY (TBI)	

Amnesia and *memory loss* are common terms for disturbances of memory. Amnesia is the inability to recall past information or to remember information relevant to the future, such as appointments. Amnesia may result from the inability to

retrieve existing memories or to store new memories, and may be temporary (such as following CONCUSSION) or permanent. Memory loss is an imprecise term that usually refers to the permanent inability to retrieve information from long-term memory.

Symptoms and Diagnostic Path

It is normal for people to forget recent information such as where they placed the car keys or phone numbers they use infrequently. Forgetfulness crosses the line to memory impairment when a person cannot remember information essential for daily activities, such as familiar faces and names or where he or she lives. The diagnostic path includes a comprehensive medical examination, neurologic examination, and imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN to identify possible organic causes within the brain. Functional magnetic resonance imaging (fMRI), a dynamic variation of MAGNETIC RESONANCE IMAGING (MRI) that shows the functional activity of the brain, may show areas of diminished activity during memory tasks. Memory and cognitive tests help identify the kinds of memory affected and define remaining memory functions.

Treatment Options and Outlook

Treatment for memory impairment depends on the underlying cause. Memory functions lost due to injury or infection such as encephalitis often return as the brain heals. The return commonly takes place in fragments, often with older memories (such as from childhood) emerging first. Memory impairment due to conditions such as stroke or Alzheimer's disease is generally permanent. Medications such as the acetylcholinesterase inhibitors doctors prescribe to treat Alzheimer's disease improve memory and cognition in many people in the early to middle stages of the condition though do not appear especially effective in treating memory impairment resulting from other causes. Permanent memory impairment may also be progressive, as occurs with degenerative conditions such as Alzheimer's disease and PARKINSON'S DISEASE.

Exercising memory and cognition, such as with crossword puzzles and other activities that require storage and recall of information, helps keep these abilities as functional as possible in healthy aging as well as when health conditions exist that have the potential to impair memory. Memory specialists can help individuals develop methods and approaches to maintain optimal memory capability as well as to accommodate memory impairment. The herbal products GINKGO BILOBA and GINSENG may improve circulation to the brain, resulting in overall improvement of memory and cognitive functions.

Risk Factors and Preventive Measures

Diseases, systemic and neurologic, and injuries to the brain are the primary risk factors for memory impairment. To a great extent, injuries to the brain that might result in impaired memory are preventable through safety measures, such as wearing appropriate protective headgear and avoiding activities with a high risk for head injury. Lifestyle factors influence some conditions that can cause memory impairment, such as HEART ATTACK and stroke. Chronic ALCOHOLISM contributes to episodic as well as progressive memory loss. Family history may be a risk factor for neurologic conditions such as Alzheimer's disease and dementia, for which there are no known measures of prevention.

See also ACCIDENTAL INJURIES; AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; ANTI-AGING APPROACHES; ARTERIOSCLEROTIC PLAQUE; COGNITIVE FUNCTION AND DYSFUNCTION; HYPNOSIS; LEARNING DISORDERS; NEURON; POST-TRAUMATIC STRESS DISORDER (PTSD).

meninges The connective tissue membranes that enclose and protect the BRAIN and SPINAL CORD (collectively called the CENTRAL NERVOUS SYSTEM). There are three meninges:

- The dura mater is the tough, outermost meninx. It has two layers, a fibrous outer layer that attaches to the inside of the cranium (skull bones) and a soft inner layer that contains an extensive network of BLOOD vessels. The dura mater sometimes folds back on itself (dural reflections) or its layers separate to form pockets (dural sinuses).
- The arachnoid mater is the middle meninx.
- The innermost meninx is the pia mater, a tissue-like membrane that covers the surface of the brain.

CEREBROSPINAL FLUID circulates between the arachnoid mater and the pia mater, in an envelope-like pocket called the subarachnoid space.

DURA MATER GRAFTS AND CJD

For several decades neurosurgeons have used grafts of dura mater acquired from cadaver donors to replace dura mater removed during neurosurgery or in circumstances of extensive injury to the BRAIN. In the late 1990s researchers traced several cases of CREUTZFELDT-JAKOB DISEASE (CJD) to the grafts, which had been harvested from individuals who turned out to have CJD. US Food and Drug Administration (FDA) regulations now establish strict criteria for the harvesting and processing of dura mater grafts to reduce the risk of transmitting infectious conditions such as CJD.

For further discussion of the meninges within the context of the structures and functions of the NERVOUS SYSTEM, please see the overview section "The Nervous System."

See also MENIGITIS.

multiple sclerosis A chronic, progressive demyelinating disorder that affects the CENTRAL NERVOUS SYSTEM (BRAIN and SPINAL CORD) and the CRANIAL NERVES, notably the optic nerves. Though the cause of multiple sclerosis remains unknown, most researchers believe the condition is an autoimmune disorders in which the body's IMMUNE RESPONSE attacks myelin, the fatty substance that coats nerves. The areas under attack become inflamed and separate from the nerves, and as they heal scars form. Over time the SCAR tissue damages the nerves and disrupts the passage of electrical impulses. The progression of demyelination is generally slow, occurring over several decades. There is wide variation in the severity of multiple sclerosis among individuals. Some people experience few symptoms and negligible interference with their regular activities and other people lose control of muscles and mobility.

Symptoms and Diagnostic Path

One of the earliest signs of multiple sclerosis is RETROBULBAR NEURITIS, an INFLAMMATION of the OPTIC NERVE (second cranial NERVE) that impairs vision. Indications of retrobulbar neuritis include DIPLOPIA (double vision), blurred vision, impaired color vision and scotomas (blind spots in the field of vision). Other symptoms are neurologic and include

- weakness and lack of coordination in the arm or leg on one side of the body
- gait disturbances such as stumbling
- transient PARESTHESIA (tingling or numbness that comes and goes without apparent cause) on one side of the body
- intermittent loss of BLADDER control (URINARY INCONTINENCE)
- emotional lability
- VERTIGO and dizziness
- fatigue
- SEXUAL DYSFUNCTION (notably ERECTILE DYSFUNCTION in men)

Because symptoms are typically transient they often occur over a number of years before a person seeks medical attention for them. The diagnosis is primarily one of exclusion so the diagnostic path includes a general medical examination, BLOOD tests, NEUROLOGIC EXAMINATION, LUMBAR PUNCTURE, and imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) of the brain to rule out other potential causes, such as BRAIN TUMOR, of symptoms. Imaging procedures, especially MRI, also may show the lesions (scarring) that characterize multiple sclerosis. However, there is no conclusive diagnostic test for multiple sclerosis and a person may seek medical care for a number of years before doctors feel confident making the diagnosis.

Heat often worsens the symptoms of multiple sclerosis. For this reason, doctors advise against hot tubs, saunas, exposure to hot weather, and hot showers or baths.

Treatment Options and Outlook

For most people the course of multiple sclerosis is one of alternating relapse and REMISSION, without predictability for the frequency or duration of either. Treatment depends on the severity and frequency of symptoms. People who have mild

MEDICATIONS TO TREAT MULTIPLE SCLEROSIS

Drug or Medication	Course of Action	Concerns/Side Effects
interferon beta 1a (Rebif) interferon beta 1b (Betaseron)	genetically engineered proteins that direct IMMUNE SYSTEM responses against viruses enhances natural immune function	may cause development of antibodies NAUSEA, VOMITING, MUSCLE aches (flu-like symptoms) requires weekly intramuscular injections
glatiramer (Copaxone)	block IMMUNE RESPONSE from attacking myelin alternative to beta INTERFERONS	flushing, shortness of breath requires daily subcutaneous injection
corticosteroids (prednisone, prednisolone, dexamethasone)	suppress immune response reduce INFLAMMATION	HYPERTENSION OSTEOPOROSIS increased risk for INFECTION
selective serotonin reuptake inhibitor (SSRI) antidepressants (fluoxetine, sertraline, venlafaxine, parocetine)	stabilize emotions reduce DEPRESSION	drowsiness, dry MOUTH, sexual side effects interactions with other medications cannot take with tricyclic antidepressants
tricyclic antidepressants (amitriptyline, nortriptyline, imipramine, doxepin)	reduce PAIN reduce DEPRESSION	drowsiness, dry mouth, sexual side effects interactions with other medications cannot take with SSRI antidepressants
muscle relaxants (baclofen, tizanidine, diazepam, clonazepam)	reduce muscle spasms	drowsiness muscle weakness
BOTULINUM THERAPY	spasticity that does not respond to other treatment temporarily paralyzes muscles into which it is injected	may cause weakness in injected muscles
ANTIVIRAL MEDICATIONS (acyclovir, Famvir, valacyclovir, amantadine)	improve immune system response to viruses	may slow attacks
modafinil	reduce drowsiness	HEADACHE difficulty sleeping
ANALGESIC MEDICATIONS (acetaminophen, NONSTEROIDAL ANTI-INFLAMMATORY DRUGS [NSAIDS])	relieve pain reduce inflammation	STOMACH irritation (NSAIDS)
mitoxantrone (Novantrone)	CHEMOTHERAPY agent slows attacks on myelin extends periods of remission	intravenous injection every three months for up to three years nausea, vomiting muscle aches may increase risk for cardiovascular disease

episodes of symptoms with extended period of remission, treatment may consist of watchful waiting and approaches to relieve symptoms that become troublesome. People who have moderate to severe episodes of symptoms with short periods of remission may improve with medications specifically for multiple sclerosis. Because these medications have significant side effects, cannot reverse neurologic damage that has already occurred, or halt the progression of multiple sclerosis, doctors reserve their use for people whose symptoms are debilitating. Other medications can suppress the body's immune response, helping slow the attacks.

Lifestyle factors such as nutritious EATING HABITS and daily physical activity help maintain motor functions and coordination. WEIGHT LOSS AND WEIGHT MANAGEMENT are essential for people who have multiple sclerosis, as maintaining appropriate body weight reduces the workload of the muscles. Regular physical exercise also helps to counter DEPRESSION. Most people are able to continue with physical activities they enjoyed before developing multiple sclerosis. Because heat exacerbates symptoms, people who live in warmer climates may want to use the cooler early morning or late evening hours for physical activities outdoors, and use indoor air-conditioned facilities at other times. Swimming provides good aerobic conditioning as well as the opportunity to strengthen weakened muscles in an environment of reduced resistance.

Though it is progressive, multiple sclerosis generally does not cause death or shorten life expectancy. Most people who have multiple sclerosis are able to participate in the work and leisure activities they enjoy when the condition is in remission, and periods of remission may last 10 years or longer. People who have more aggressive forms of multiple sclerosis may progress to assisted mobility within a shorter period of time than people who have the more classic, slowly progressive forms of the condition.

Risk Factors and Preventive Measures

Multiple sclerosis affects twice as many women as men and most commonly makes its first appearance between the ages of 20 and 40 years. It is likely that external environment (such as climate) and genetics both influence the development of multiple sclerosis, as the condition is far less common in tropical regions of the world and more likely to occur when other family members have the condition. However, researchers do not fully understand the connections among these factors. Some researchers believe there may also be involvement of an as yet undetected VIRUS. There are no known measures for preventing multiple sclerosis.

See also AMYOTROPHIC LATERAL SCLEROSIS (ALS); AUTOIMMUNE DISORDERS; GENETIC PREDISPOSITION; LESION; SCAR; SCOTOMA.

myoclonus Involuntary and episodic contractions, twitching, or spasms of MUSCLE groups. Harmless manifestations of myoclonus include brief HICCUPS or the rapid jerking people may experience when falling asleep (sometimes called sleep starts). Myoclonus also may be a symptom of injury to motor neurons, to the NERVE cells in the SPINAL CORD that direct voluntary movement, or to parts of the BRAIN that participate in movement. Myoclonus occurs as rapid, jolt-like episodes and may take various forms that include the following:

- Action myoclonus occurs or intensifies during attempts at voluntary movement, such as walking or eating. It most commonly develops after circumstances of extended oxygen deprivation to the brain (HYPOXIA), such as may occur with STROKE, HEART ATTACK, or near drowning.
- Essential myoclonus is not associated with any detectable neurologic injury or dysfunction to account for the symptoms.
- Stimulus-sensitive myoclonus occurs as an apparent HYPERSENSITIVITY REACTION (neurologic) to external stimuli, such as sounds and lights.
- Sleep myoclonus occurs when sleep starts become excessive and disruptive to sleep. Some neurologists believe sleep myoclonus is a form of stimulus-sensitive myoclonus in which the person may or may not recognize the external stimuli that trigger the myoclonic episodes.
- Cortical reflex myoclonus, reticular reflex myoclonus, and progressive myoclonus epilepsy, are SEIZURE DISORDERS that include myoclonus among their symptoms.

- Palatal myoclonus occurs when the muscles of the soft palate at the back of the MOUTH contract rapidly and rhythmically though usually without disrupting the ability to swallow or speak.

The pattern and consistency of the myoclonic episodes help the neurologist determine the underlying cause or location of the neurologic injury (sometimes called a LESION). The diagnostic path typically includes a comprehensive NEUROLOGIC EXAMINATION and imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN to locate or rule out neurologic damage. The neurologist may also conduct an electromyogram (EMG) to assess the activity of the affected muscle groups. Treatment aims to reduce the symptoms and typically includes combinations of muscle relaxants and antiseizure medications. Finding a therapeutically effective balance of medications is often a trial-and-error process. Most people who have myoclonus require lifelong treatment.

CONDITIONS IN WHICH MYOCLONUS MAY OCCUR

ALZHEIMER'S DISEASE	BRAIN HEMORRHAGE
BRAIN TUMOR	CREUTZFELDT-JAKOB DISEASE (CJD)
ENCEPHALITIS	MULTIPLE SCLEROSIS
PARKINSON'S DISEASE	prolonged HYPOXIA
SEIZURE DISORDERS	SPINAL CORD INJURY
STROKE	TRAUMATIC BRAIN INJURY (TBI)

See also ATHETOSIS; CHOREA; NEURON; RESTLESS LEGS SYNDROME; SPASM; TIC; TOURETTE'S SYNDROME; TREMOR DISORDERS.

N–O

narcolepsy A sleep disorder in which a person feels chronically tired and sleep deprived, and may experience uncontrollable episodes of falling asleep during the day. People who have narcolepsy have disturbed sleep patterns while falling asleep, often experiencing premature sleep PARALYSIS (an inability to move which normally occurs in rapid eye movement [REM] sleep as a protective mechanism to keep the body from enacting dreams), hypnagogic hallucinations (inability to distinguish between dreamlike images and reality when falling asleep), and daytime cataplexy (sudden, brief episodes of MUSCLE weakness or inability to move). As well, the person experiences abnormal and very short REM sleep periods (detected through diagnostic sleep studies) that prevent restful sleep. Researchers believe narcolepsy is far more common than diagnosis data suggest because many people do not seek medical evaluation or treatment.

The diagnostic path includes a general medical examination and basic NEUROLOGIC EXAMINATION to evaluate overall health and neurologic function. Diagnostic sleep studies reveal the characteristic traits of narcolepsy, distinguishing the disorder from other SLEEP DISORDERS. Treatment is a combination of medications that may include

- AMPHETAMINES (STIMULANTS) to diminish daytime sleepiness
- modafinil, a nonamphetamine DRUG that targets different BRAIN functions from amphetamines to improve daytime alertness
- sleep medications such as flurazepam and other benzodiazepine drugs to encourage relaxation when falling asleep
- tricyclic antidepressants such as imipramine and desipramine to improve REM sleep

Some people also benefit from scheduled short naps throughout the day, which may provide restful sleep as well as decrease feelings of sleepiness. Researchers do not know what causes narcolepsy, though there is some evidence that it may be an AUTOIMMUNE disorder because there seems to be involvement of HUMAN LEUKOCYTE ANTIGENS (HLAS), which are fundamental to the IMMUNE RESPONSE. There is also some evidence that people who have narcolepsy have reduced levels of a neuroprotein called hypocretin. However, researchers do not know what these correlations mean or how they cause narcolepsy. Narcolepsy is a lifelong condition.

See also APNEA; AUTOIMMUNE DISORDERS; RESTLESS LEGS SYNDROME.

nerve An organization of connected neurons that conducts electrical impulses, typically forming the structure of a fiber. The nerve fibers may be microscopic, such as the nerves that carry impulses from the fingertips to the BRAIN, or clearly visible to the EYE, such as the SPINAL CORD. The PERIPHERAL NERVES originate in the brain, brainstem, and SPINAL CORD and extend to their destinations in the body. A cluster or mass of nerves located outside the CENTRAL NERVOUS SYSTEM (brain and spinal cord) is a ganglion.

For further discussion of nerves within the context of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also DIABETES; NEURALGIA; NEURITIS; PERIPHERAL VASCULAR DISEASE (PVD).

nerve cell See NEURON.

nervous system The BRAIN and network of nerves that convey electrical impulses to and from

all structures in the body. The two major divisions of the nervous system are the CENTRAL NERVOUS SYSTEM and the PERIPHERAL NERVOUS SYSTEM. The central nervous system consists of the brain and SPINAL CORD. The peripheral nervous system consists of all other NERVE structures, including the CRANIAL NERVES, the SPINAL NERVES, and the PERIPHERAL NERVES.

For further discussion of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also NEURON; NEURORECEPTOR; NEUROTRANSMITTER.

neuralgia PAIN that occurs along a DERMATOME (the tract of a NERVE). Neuralgia is often severe, sharp, and brief (each episode lasting 15 seconds or less) though repetitive. The most common causes of neuralgia are INFECTION (notably HERPES ZOSTER, also called postherpetic neuralgia) and compression (a "pinched" nerve). DIABETES, untreated (tertiary) SYPHILIS, MULTIPLE SCLEROSIS, and PORPHYRIA are among the health conditions that can cause neuralgia. Exposure to toxins, notably heavy metals such as arsenic and lead, may cause certain forms of neuralgia. Often, however, the doctor cannot identify the cause of neuralgia. Neuralgia may affect any dermatome in the body. Those most often affected are the CRANIAL NERVES that serve the face and head (especially the glossopharyngeal, trigeminal, facial, and occipital), the intercostal nerves (ribs), and the posterior tibial nerve (ankle and foot).

Symptoms and Diagnostic Path

Neuralgia typically begins with sudden, sharp pain along the affected dermatome. The attacks may be momentarily disabling and last 10 to 15 seconds. However, a person may experience dozens of sequential attacks in episodes, with periods of REMISSION during which there is no pain. The pain is

- always in the same location
- near the surface rather than deep in the body
- often intense and intermittent, though sometimes continuous

Sometimes touching a particular area on the SKIN or actions, such as chewing trigger, attacks of pain. The diagnostic path includes a NEUROLOGIC EXAMINATION and often electromyogram (EMG) to assess the function of the nerves in the affected area. The neurologist may conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to determine whether there is compression of the affected nerve, such as from a tumor, or to rule out other possible causes of the pain.

Treatment Options and Outlook

Treatment targets the cause when known, such as PHYSICAL THERAPY or surgery to relieve compression against a nerve, removal from exposure to potential toxins, or ANTIVIRAL MEDICATIONS for postherpetic neuralgia. Tricyclic antidepressants are particularly effective for relieving the pain of trigeminal neuralgia. Other medications to relieve pain include nonnarcotic and narcotic oral ANALGESIC MEDICATIONS, topical analgesics such as capsaicin, certain antiseizure medications, topical lidocaine patches, corticosteroid/lidocaine injections as neural blockades (nerve blocks) and TRIGGER-POINT INJECTION. These and other treatments can provide relief from the symptoms of neuralgia for most people. Taking medications, even narcotic analgesics, on a regular schedule is usually more effective than waiting until pain occurs or becomes intolerable. ACUPUNCTURE and BIOFEEDBACK are also effective for some people.

Postherpetic neuralgia generally improves and often resolves (goes away) within 2 to 12 months as the underlying damage to the involved dermatome heals. Neuralgia due to other causes may persist, particularly if the cause is chronic (such as diabetes or MULTIPLE SCLEROSIS). When medications and other therapies cannot control the pain (intractable neuralgia), the neurologist or pain specialist may recommend RHIZOTOMY, a surgical OPERATION to cut the nerve rootlets responsible for conducting the pain impulses. Such intervention usually, though not always, ends the pain though may also alter sensory perception along the dermatome.

Risk Factors and Preventive Measures

Age is the most significant risk factor for neuralgia, particularly postherpetic neuralgia. Reduced immune function, especially in people who have HIV/AIDS or take IMMUNOSUPPRESSIVE THERAPY such as

after ORGAN TRANSPLANTATION, allows the dormant varicella-zoster VIRUS to emerge and cause shingles. Injuries to the nerves, such as repetitious motion and compression injuries, also become more common with advancing age.

Antiviral medications, such as acyclovir or famciclovir, taken within 72 hours of the onset of herpes zoster symptoms may be effective in preventing postherpetic neuralgia. Without antiviral therapy, about 20 percent of people who develop herpes zoster infection subsequently develop postherpetic neuralgia. The extent to which antiviral therapy for the herpes zoster affects the likelihood of developing postherpetic neuralgia remains unknown. Other preventive measures include prompt treatment of NEURITIS (INFLAMMATION of a nerve), appropriate intake of vitamin B_{12} (which is vital for proper nerve function), and avoidance of toxins that can damage the nerves.

See also AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; HEADACHE; HEAVY-METAL POISONING; NEURAL BLOCKADE (NERVE BLOCK); NEUROPATHY.

neuritis INFLAMMATION of a NERVE. Neuritis is usually an indication of an underlying injury or disease process such as irritation, compression, or INFECTION of the involved nerve. The most common symptom is PARESTHESIA (tingling) though some people may experience PAIN (NEURALGIA) or numbness. The diagnostic path is primarily clinical, based on the person's symptoms and a NEUROLOGIC EXAMINATION. PAPILLITIS and RETROBULBAR NEURITIS, inflammations involving different parts of the OPTIC NERVE, can result in vision loss. Retrobulbar neuritis can be an early sign of MULTIPLE SCLEROSIS. Treatment targets the underlying cause and may include anti-inflammatory medications or ANTIBIOTIC MEDICATIONS; when the cause is compression due to an entrapment syndrome (such as CARPAL TUNNEL SYNDROME), surgery may be necessary to relieve the compression.

See also SCIATICA.

neurofibromatosis A genetic disorder in which tumors (neurofibromas) form within the tissues and structures of the NERVOUS SYSTEM. There are two primary forms of neurofibromatosis, both of which occur in an autosomal dominant INHERITANCE PATTERN. The tumors, notably those that involve the SKIN, are initially benign (noncancerous) though have a high risk for turning cancerous. Neurofibromatosis type 1 (NF-1) is the more common form; it generates dozens of tiny tumors. Neurofibromatosis type 2 (NF-2) primarily involves the SPINAL CORD and eighth cranial NERVE (vestibulocochlear nerve). Both forms of neurofibromatosis may also involve the BONE, skin, MUSCLE, and connective tissue as well as the BRAIN and the visceral organs.

The earliest sign of neurofibromatosis is often lightly colored patches of skin (café au lait macules). Many people who have NF-1 develop numerous small growths that look like moles (nevi). However, it is possible to press these tumors below the surface of the skin as though turning them into themselves (called a buttonhole effect), whereas moles and similar growths are firm and remain above the skin's surface when pressed. Tumors of NF-2 that arise in the spinal cord may cause deformity of the spine and SCOLIOSIS.

Because the neurofibromas often develop within the tissues of the brain, other symptoms may include seizures, intellectual impairment, and disturbances of motor function. Other symptoms depend on the locations of the tumors. The diagnostic path includes a comprehensive FAMILY MEDICAL HISTORY; immediate family members who have similar symptoms or a diagnosis of neurofibromatosis make the diagnosis fairly conclusive. A NEUROLOGIC EXAMINATION and imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and COMPUTED TOMOGRAPHY (CT) SCAN of the brain may reveal tumors.

The preferred treatment is surgery to remove the tumors whenever practical, and close monitoring of tumors that the surgeon cannot remove to assess any changes that could indicate developing malignancies. Unfortunately the tumors tend to recur. Left untreated, however, the tumors often cause deformity of the tissues and structures in which they are growing. As well, the risk for malignancy is very high. Health experts strongly recommend GENETIC COUNSELING for people diagnosed with neurofibromatosis.

See also ACOUSTIC NEUROMA; BRAIN TUMOR; CRANIAL NERVES; GENETIC DISORDERS; MACULE; NEVUS; PHEOCHROMOCYTOMA.

neurologic examination A series of basic diagnostic procedures that help the neurologist assess an individual's neurologic status. A fundamental dimension of the neurologic examination is observation, through which the neurologist can gain much information about a person's mental status (cognition and memory), motor function (balance, coordination, STRENGTH), and sensory perception (touch, vision, hearing). Specific procedures include testing the reflexes, response to specific sensory stimuli (soft touch, PAIN, vibration, particular smells or tastes), and the ability to carry out directed movements (such as tracking the movement of an object or touching specific body locations). The neurologist generally performs basic tests of VISUAL ACUITY and field of vision, hearing, and examination of the inner EYE.

Basic assessment of cognitive function and memory may include reading, spelling, and drawing activities. Tasks such as unbuttoning and buttoning, writing one's signature, and handling small objects test dexterity and fine motor movement. The ways in which a person stands, walks, and rises from and lowers to sitting and prone positions help the neurologist further assess MUSCLE strength, coordination, and PROPRIOCEPTION (awareness of the body's position relative to its environment). The neurologist may conduct other evaluations and procedures, including more extensive cognitive testing, depending on basic findings. A basic neurologic examination may take about 20 minutes for the neurologist to complete.

See also COGNITIVE FUNCTION AND DYSFUNCTION; MEMORY AND MEMORY IMPAIRMENT; REFLEX.

neuron A NERVE cell. A neuron consists of a cell body, nucleus containing the cell's DNA, cytoplasm, organelles (structures within the cytoplasm that conduct functions such as energy production), axons (fibers that carry nerve impulses away from the neuron), and dendrites (rootlike structures that receive the nerve impulses). A myelin sheath (coating of myelin, a fatty substance) may enclose a neuron's axon, insulating it to maintain the integrity of the nerve impulses the axon carries. Dendrites do not have myelin sheaths. An axon may extend several inches to several feet, while dendrites remain close to the neuron's cell body. Axons and dendrites extend into spaces around the neurons called synaptic corridors. The end of the axon branches into numerous extensions called presynaptic terminals. The gap between an axon of one neuron and the dendrites of another neuron is a synapse.

Neurons communicate (conduct nerve impulses) through an electrochemical process called action potential, an exchange of electrically charged particles (ions) across the cell's membrane. A neuron at rest contains a negative charge within its membrane though the environment outside the cell membrane carries a positive charge. A nerve impulse creates a surge or spike of electrical energy that causes ion channels in the cell membrane to open. At the same time the neuron releases a chemical messenger, a NEUROTRANSMITTER.

The neurotransmitter binds with the appropriate NEURORECEPTOR on the dendrites of the neuron intended to receive the nerve impulse. The type of neuron—for example, motor or sensory—determines which neurotransmitters and neuroreceptors are present. As the neuron's polarity changes (the neuron achieves action potential), the electrical impulse moves to the neuron. The process takes only a minuscule fraction of a second to complete. An enzyme then initiates reuptake (recycling) of the neurotransmitter, setting the stage for the next cycle. Neurons align in neuronal pathways that facilitate the conduction of nerve impulses for optimal efficiency.

Neurons are the oldest cells in the body. Most develop in the early to middle stages of gestation, with the final surge of neuron production taking place shortly before birth. The body's full complement of neurons is present at birth, the majority of which survive and function for the course of a full lifetime. The body cannot replace neurons that die, and neurons do die at a fairly consistent rate, barring injury or disease, of about one per day throughout life.

See also CELL STRUCTURE AND FUNCTION.

neuropathy Dysfunction of or damage to the PERIPHERAL NERVES. Neuropathy may be temporary or permanent and may result from numerous causes, such as INFECTION, compression, degenerative disease processes, and AUTOIMMUNE DISORDERS. Neuropathy may involve only a single peripheral

NERVE (as in compression) or multiple peripheral nerves, either in a pattern (as in RAYNAUD'S SYNDROME or shingles) or diffusely throughout the body (as in neuropathy of DIABETES). Neurologists classify the more than 100 forms of neuropathy into broad categories according to the type of nerve affected—motor, sensory, mixed, and autonomic.

The symptoms of neuropathy vary widely with the nerves affected and extent of the condition causing the neuropathy. PAIN, MUSCLE weakness or loss of muscle function, disturbances of sensory perception, and dysfunction of autonomic processes such as digestion are among the myriad symptoms that can occur with neuropathy. The diagnostic path typically seeks to identify the underlying cause of the damage, which then becomes the target for treatment methods. Some neuropathies resolve (go away) with appropriate treatment, though often there is some residual damage as the nerves are delicate and the body cannot replace neurons that die.

Because pain is a common symptom of neuropathy, treatment often includes medications such as analgesics, tricyclic antidepressants, certain antiseizure medications, injected anesthetics and corticosteroids, and topical anesthetics or analgesics (lidocaine or capsaicin). Surgery may be appropriate to relieve compression against a nerve or to sever the nerve when other treatments fail to relieve incapacitating pain. Noninvasive approaches to pain management that are sometimes effective include BIOFEEDBACK and ACUPUNCTURE.

CONDITIONS THAT CAN CAUSE NEUROPATHY

chronic CIRRHOSIS	CYTOMEGALOVIRUS (CMV)
DIABETES	EPSTEIN-BARR VIRUS
GENETIC DISORDERS	GUILLAIN-BARRÉ SYNDROME
Hansen's disease	HEAVY-METAL POISONING
HIV/AIDS	HYPOTHYROIDISM
long-term ALCOHOLISM	LYME DISEASE
MULTIPLE SCLEROSIS	NEUROFIBROMATOSIS
PERIPHERAL VASCULAR DISEASE (PVD)	RAYNAUD'S SYNDROME
RENAL FAILURE	REPETITIVE motion INJURIES
SCIATICA	shingles
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	traumatic injury
VASCULITIS	vitamin B_{12} deficiency

See also ALTERNATIVE METHODS FOR PAIN RELIEF; CRANIAL NERVES; NEURALGIA; NEURITIS; RETROBULBAR NEURITIS; RHIZOTOMY; SPINAL NERVES.

neuroreceptor A molecular structure on the surface of a cell membrane that accepts (binds with) a NEUROTRANSMITTER (chemical messenger). Nearly always a neuroreceptor is specific for only one neurotransmitter. The common analogy is that a neuroreceptor functions like a lock and a neurotransmitter functions like a key; only the correct key can open the lock. Neuroreceptors tend to align along the cell membrane such that they match across cells, facilitating communication between cells. Most cells contain numerous and different neuroreceptors. Drugs may also bind with neuroreceptors, causing an effect (partial or complete) that emulates that of the matching neurotransmitter (agonist) or that blocks the neuroreceptor from accepting the neurotransmitter (antagonist). Some neuroreceptors have multiple binding sites that accept different chemicals (such as neurotransmitters, drugs, and ions).

For further discussion of neuroreceptors within the context of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also ADDICTION; PARKINSON'S DISEASE.

neurotransmitter A chemical that facilitates the passage of NERVE impulses among neurons. A neurotransmitter may allow or block the travel of a nerve impulse. Neurons store the chemical components of their neurotransmitters in microscopic structures called the synaptic vesicles, synthesizing the appropriate neurotransmitter when conducting a nerve impulse. The sending NEURON's axon releases the neurotransmitter into the synapse (space between neurons). The neurotransmitter crosses the synapse to bind with the appropriate NEURORECEPTOR on the dendrites of the receiving

NEUROTRANSMITTERS

acetylcholine	aspartate
DOPAMINE	EPINEPHRINE
gamma-aminobutyric acid (GABA)	glutamate
monoamine oxidase (MAO)	NOREPINEPHRINE
serotonin	

neuron. Hormones may also function as neurotransmitters.

The appropriate balance of neurotransmitters is essential for neurologic function, as some neurotransmitters are excitory (allow nerve impulses to move from one neuron to another) and others are inhibitory (block nerve impulses). Neurotransmitters have specific functions. The BLOOD–BRAIN BARRIER allows the NERVOUS SYSTEM to maintain different levels of neurotransmitters in the BRAIN and in the body. Acetylcholine, for example, is essential in the brain for functions of cognition and memory. A diminished level of acetylcholine in the brain is among the hallmark characteristics of ALZHEIMER'S DISEASE. DOPAMINE is critical for movement; PARKINSON'S DISEASE develops when the cells in the brain that produce dopamine die. Dopamine also facilitates nerve impulses that activate the brain's pleasure centers. Monoamine oxidase (MAO), serotonin, and NOREPINEPHRINE are key to mood. ANTIDEPRESSANT MEDICATIONS act by altering the balance of these three chemicals in the brain. In the body, acetylcholine conducts electrical impulses between neurons and MUSCLE cells to facilitate movement. EPINEPHRINE and norepinephrine conduct electrical impulses in the HEART.

For further discussion of neurotransmitters within the context of the structures and functions of the nervous system, please see the overview section, "The Nervous System."

See also AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; HORMONE.

organic brain syndrome A collective term for disorders of cognition (thought and logic) and memory that arise from physical changes that take place in the BRAIN. Numerous neurologic and metabolic disorders can cause organic brain syndrome, as can head trauma and INFECTION, such as ENCEPHALITIS. Organic brain syndrome sometimes becomes an ambiguous diagnosis when there are few distinct or apparent causes to explain mental deterioration in people who are elderly. However, the physical changes that occur in the brain to produce organic brain syndrome are more common in old age though are not inevitable aspects of aging.

COMMON DISORDERS ASSOCIATED WITH ORGANIC BRAIN SYNDROME

ALZHEIMER'S DISEASE	DEMENTIA
ENCEPHALITIS	HEART ATTACK
hepatic NEUROPATHY	HUNTINGTON'S DISEASE
HYDROCEPHALY	HYPOXIA
long-term ALCOHOLISM	MENINGITIS
PARKINSON'S DISEASE	SEPTICEMIA
STROKE	substance abuse
TRANSIENT ISCHEMIC ATTACK (TIA)	TRAUMATIC BRAIN INJURY (TBI)

Symptoms and Diagnostic Path

The presentation and severity of symptoms varies with the underlying condition and other health factors. Symptoms extend over time and often worsen with time. Key symptoms include

- confusion, disorientation, and DELIRIUM
- difficulty carrying out tasks that require thought, logic, and reasoning such as shopping or traveling to and from home
- diminished ability to interact with others in social settings
- diminished ability to independently carry out activities of daily living such as bathing, dressing, and preparing meals
- lapses of memory, especially inability to remember recent events

The diagnostic path begins with a ROUTINE MEDICAL EXAMINATION to assess health overall and a NEUROLOGIC EXAMINATION to evaluate brain function and cognitive abilities. Because symptoms can result from electrolyte imbalance, HORMONE disturbances, high or low BLOOD GLUCOSE (sugar) levels, and other factors, the routine medical examination typically includes a complete blood count (CBC) and other blood tests. The doctor may also conduct a basic cardiovascular evaluation, including ELECTROCARDIOGRAM (ECG) and measurement of BLOOD PRESSURE. A number of health conditions that can cause cognitive disturbances become more common with advanced age, some of which are easily treatable such as HYPOTHYROIDISM, HYPERTENSION, ADRENAL INSUFFICIENCY, and cardiac ARRHYTHMIA. The doctor may also conduct diagnostic imaging procedures such as COMPUTED TOMOGRA-

PHY (CT) SCAN OR MAGNETIC RESONANCE IMAGING (MRI) to evaluate the brain and its blood flow.

Treatment Options and Outlook

Treatment targets the underlying condition when appropriate and otherwise focuses on maintaining QUALITY OF LIFE. Recent research shows that daily physical activity such as walking may slow the progression of disorders such as ALZHEIMER'S DISEASE and other degenerative disorders that produce organic brain syndrome symptoms. Adequate nutrition is also essential. Medications such as antidepressants and antipsychotics may help moderate behaviors and improve the person's sense of well-being. Medications to treat Alzheimer's disease, called acetylcholinesterase inhibitors, may improve cognitive ability or at least delay the progression of its decline. Because organic brain syndrome tends to be progressive, family members need to plan for ongoing care and support.

Risk Factors and Preventive Measures

Organic brain syndrome is most common among people 70 years of age and older because many of the conditions that produce the symptoms of organic brain syndrome become more common with advanced age. Mitigating the risk factors for these conditions, which range from CARDIOVASCULAR DISEASE (CVD) to DIABETES to chronic LIVER disease, reduces the likelihood for developing cognitive impairments due to physical changes in the brain. Lifestyle measures such as nutritious EATING HABITS, daily physical activity, not smoking, and maintaining healthy weight further contribute to neurologic as well as overall health. Activities that make use of logic and reasoning, such as reading and crossword puzzles, may help maintain mental acuity.

See also AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; COGNITIVE FUNCTION AND DYSFUNCTION; END OF LIFE CONCERNS; GENERATIONAL HEALTH-CARE PERSPECTIVES; MEMORY AND MEMORY IMPAIRMENT.

P

pallidotomy A surgical procedure in which the neurosurgeon destroys a portion of the globus pallidus, a structure of the midbrain that participates in regulating motor movement. Researchers in the 1950s discovered that pallidotomy could significantly reduce symptoms of PARKINSON'S DISEASE such as MUSCLE rigidity, DYSKINESIA, and gait freezing (akinesia). Until recent advances in technology, however, the risks of the surgery were greater than the benefits. Current neurosurgery techniques use MAGNETIC RESONANCE IMAGING (MRI) to locate the globus pallidus and precisely guide the insertion and placement of a thin probe the neurosurgeon uses to ablate (destroy) a few cells at a time until the OPERATION achieves the desired result. This minimizes the risk of damage to adjacent structures of the BRAIN. The person remains conscious and responds with movements as the neurosurgeon directs.

The first step of the surgery is the placement of a stereotactic halo, a circular brace attached to the skull (done under local anesthetic). The halo holds the instruments in precise position during the operation. The second step of the surgery is the ablation, or destruction of tissue in the globus pallidus. After injecting a local anesthetic to numb the SKIN and periosteum covering the cranium, the only areas that contain nerves sensitive to PAIN, the neurosurgeon drills a tiny hole and inserts the probe, feeding it slowly to the globus pallidus with MRI visualization. The operation takes 45 to 90 minutes, with improvement apparent immediately. The neurosurgeon removes the stereotactic halo when the operation is finished. Complications are rare; when they do occur they may include excessive bleeding, postoperative INFECTION, and visual disturbances (the path to the globus pallidus runs very near the optic tract). Most people return to full and regular activities within two weeks.

The effects of pallidotomy are permanent, though they do not affect the progression of the Parkinson's disease. As Parkinson's disease progresses, however, symptoms reemerge. Pallidotomy is not very effective as treatment for other movement disorders.

See also DEEP BRAIN STIMULATION; SURGERY BENEFIT AND RISK ASSESSMENT; TREMOR DISORDERS.

paralysis The loss of motor function as a result of damage (injury or disease) to the BRAIN or SPINAL CORD. STROKE and trauma are the most common causes of paralysis. Paralysis may also occur with INFECTION such as POLIOMYELITIS, complications of illness such as GUILLAIN-BARRÉ SYNDROME, and neurologic disorders such as AMYOTROPHIC LATERAL SCLEROSIS (ALS) and BELL'S PALSY. Paralysis may affect one side of the body (hemiplegia), the lower body (paraplegia), or the entire body (quadriplegia), depending on the location of the damage. Some paralysis is temporary, with function returning when the underlying condition resolves (such as with Bell's palsy and some kinds of BRAIN HEMORRHAGE). In other circumstances, such as when injury destroys NERVE tissue or structures, paralysis is permanent.

Symptoms and Diagnostic Path

The primary symptom of paralysis is loss of MUSCLE function. In most cases, paralysis comes on quickly. Some people also experience disturbance or loss of sensory perception, depending on the cause of the damage. The diagnostic path generally begins with COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to identify any correctable or treatable cause for the paralysis and

to assess the extent of damage. Prompt intervention is essential for recovery from conditions such as brain hemorrhage, stroke, BRAIN TUMOR, and compression of the spinal cord.

Treatment Options and Outlook

When possible, treatment attempts to remove or mitigate the source of the paralysis. Such efforts might include surgery to remove a tumor or collected BLOOD (as in subdural HEMATOMA) or other fluid that accumulates within the cranium (HYDROCEPHALY). Rapid treatment can halt and even reverse the effects of stroke due to cerebral infarction (blood clot in the brain). Once paralysis becomes permanent, the emphasis of treatment shifts to maintaining optimal function of remaining motor abilities and learning methods of accommodation. PHYSICAL THERAPY and OCCUPATIONAL THERAPY are essential dimensions of such treatment. Many people who have partial paralysis are able to return to independent living and often to their jobs and many of their favorite activities. Mobility aids such as wheelchairs, crutches, canes or walking sticks, walkers, and braces improve independence and QUALITY OF LIFE.

Risk Factors and Preventive Measures

The risk factors for paralysis are those of the underlying causes of damage to the brain and spinal cord. Traumatic injury is the most significant risk factor for people under age 30 years, particularly young men. Conditions such as stroke, neurologic disorders, and tumors become more common causes of paralysis among people age 50 years and older. Preventive measures include seat belt use, protective headgear for activities such as bicycling and downhill skiing, and prudent judgment when swimming and diving. Lifestyle choices such as nutritious EATING HABITS, not smoking, and daily physical activity help reduce the risk for conditions such as stroke. Other causes of paralysis, such as CEREBRAL PALSY or ALS, are not preventable.

See also PARKINSON'S DISEASE; SPINA BIFIDA; SPINAL CORD INJURY; TRAUMATIC BRAIN INJURY (TBI).

paresthesia The sensation of tingling or burning in a particular part or region of the body. Paresthesia is a symptom of damage, temporary or permanent, to a NERVE or group of nerves. The "pins and needles" feeling in a hand or foot that "falls asleep" is a common experience of transient, or temporary, paresthesia that results from compression of the nerves such as from the limb being tucked under the body during sleep or when sitting for an extended period without moving. CARPAL TUNNEL SYNDROME and ROTATOR CUFF IMPINGEMENT SYNDROME are among the common conditions that cause compression of the nerves through swelling and entrapment.

Pathologic paresthesia—parethesia arising from disease or injury—often occurs with PERIPHERAL VASCULAR DISEASE (PVD) or NEUROPATHY of DIABETES, conditions in which impaired BLOOD circulation causes damage to the PERIPHERAL NERVES of the hands and feet. Deficiency of B vitamins, especially B_{12}, and HEAVY-METAL POISONING (for example, arsenic or mercury) affects the myelin sheathing of nerves and commonly results in paresthesia. Paresthesia is also a symptom of numerous neurologic disorders and conditions and may occur in conjunction with NEURALGIA (PAIN along a nerve tract). Treatment for chronic or persistent paresthesia targets the underlying cause and may range from noninvasive methods such as BIOFEEDBACK and HYPNOSIS to therapeutic interventions such as medications or surgery.

See also BELL'S PALSY; MULTIPLE SCLEROSIS; SPINAL CORD INJURY; SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).

Parkinson's disease A degenerative neuromuscular disorder that results from the progressive loss of neurons within the structures of the midbrain, notably the substantia nigra, that produce DOPAMINE, a NEUROTRANSMITTER essential for MUSCLE function. The loss of muscle function affects both voluntary (movement) and involuntary (swallowing, digestion, urination) activities.

Symptoms and Diagnostic Path

Symptoms become apparent when the number of dopamine-producing cells drops to about 20 percent of normal and typically include

- resting tremor usually affecting the fingers, hands, feet, and occasionally the MOUTH
- bradykinesia (slowed movement)
- stiffness and rigidity of the muscles

- shuffling, hunched posture when walking (Parkinsonian gait)
- loss of balance, especially when changing direction during walking

Other symptoms develop as the condition progresses and may include SIALORRHEA (excessive drooling), HYPERHIDROSIS (excessive sweating), BLEPHAROSPASM, and difficulty speaking and swallowing. There is no definitive diagnostic test for Parkinson's disease, so the diagnostic path considers both personal health history and clinical findings. The neurologist may conduct imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN and MAGNETIC RESONANCE IMAGING (MRI) to rule out other causes of the symptoms, such as BRAIN TUMOR or STROKE.

Treatment Options and Outlook

Treatment targets the symptoms. Some medications replace dopamine or function as dopamine agonists to activate dopamine receptors. The antiviral medication amantadine improves symptoms in some people. Response to medications is highly individual. The neurologist chooses medication combinations according to the person's age, general health status, apparent rate of progression, and other factors. Most people take combinations of medications to address different aspects of the condition and to offset the side effects of some medications. The person eventually becomes resistant to levodopa, a dopamine precursor that currently is the only dopamine-replacement DRUG available. A person who has Parkinson's disease can typically take levodopa for five to seven years.

The US Food and Drug Administration (FDA) recently approved the surgical treatment DEEP BRAIN STIMULATION (DBS) as a treatment for Parkinson's disease that no longer responds to medications. In DBS, the neurosurgeon implants an electrode deep into the BRAIN near the thalamus (a structure with an integral role in movement and motor function). The electrodes connect to a pulse generator, similar in concept to a HEART PACEMAKER, implanted in a small pocket of tissue. The neurologist programs the pulse generator to deliver regular electrical impulses that subdue dyskinesias, rigidity, and tremors. DBS can provide relief from symptoms for a year or two with reprogramming to adjust the intervals and intensity of the electrical impulses.

Parkinson's disease typically progresses over several decades. With early treatment many people can remain symptom free for years. As the number of dopamine-producing cells in the brain continues to decline, however, medications to treat Parkinson's disease become less effective and eventually do not work at all. Though Parkinson's disease continues to progress, it is not fatal for most people when the age of onset is 60 or later.

Risk Factors and Preventive Measures

Researchers do not know what causes Parkinson's disease, though it does appear to run in some families. The most significant risk factor for Parkinson's disease is advancing age, as neurologists diagnose the condition most frequently in people who are age 60 or older. Researchers believe most early-onset Parkinson's disease, which often begins in the 30s or 40s, is genetic. There are no measures known to prevent Parkinson's disease.

See also AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; ALZHEIMER'S DISEASE; DEMENTIA; HUNTINGTON'S DISEASE; PALLIDOTOMY; THALAMOTOMY; TREMOR DISORDERS.

peripheral nerves The nerves that branch from the CENTRAL NERVOUS SYSTEM to serve the body. The primary peripheral nerves are the CRANIAL NERVES and the SPINAL NERVES, which branch into smaller and numerous nerves that extend to all parts of the body. The peripheral nerves may be visible to the unaided EYE, as are the cranial nerves and the spinal nerves, or microscopic, as are the tiny nerves that serve areas such as the fingertips. Sensory nerves carry signals to the BRAIN and motor nerves carry signals to the body. Some nerves have both functions.

For further discussion of the peripheral nerves within the context of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also SPINAL CORD.

peripheral nervous system The CRANIAL NERVES, SPINAL NERVES, and their extensions. The peripheral nervous system has two major subdivisions: the

somatic NERVOUS SYSTEM and the autonomic nervous system. The nerves of the somatic nervous system are both sensory (conduct signals from the body to the BRAIN) and motor (carry signals from the brain to the structures of the body that are under voluntary control). The nerves of the autonomic nervous system regulate involuntary functions such as HEART RATE and digestion as well as the endocrine and exocrine glands. The autonomic nervous system has two further subdivisions: the sympathetic nerves (which serve the thorax and lumbar region) and parasympathetic nerves (which serve the head and sacral region.

For further discussion of the peripheral nervous system within the context of the structures and functions of the nervous system as a whole, please see the overview section "The Nervous System."

See also CENTRAL NERVOUS SYSTEM; ENDOCRINE GLAND; PERIPHERAL NERVES.

persistent vegetative state An extended state of unconsciousness in which higher BRAIN activity (cerebral cortex function) is negligible or lost though the brainstem continues to operate to sustain the vital functions of living such as breathing, HEART RATE, and BLOOD PRESSURE. Basic motor function, such as spontaneous though undirected movement, may also occur as the brainstem is responsible for some motor functions. The person may also make sounds, move the eyes, and move the MOUTH. However, there is no recognition of or purpose to these actions, and the person cannot follow instructions to move in certain ways and does not speak, drink, or eat.

A person may remain in a persistent vegetative state for months, years, or decades with adequate nutritional support. Though in general the longer a person remains in a persistent vegetative state the less likely he or she will recover conscious function, occasionally individuals emerge after extended periods. The likelihood of recovery depends on the extent and nature of damage to the cerebral cortex, which imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and COMPUTED TOMOGRAPHY (CT) SCAN can help assess. Persistent vegetative state raises many medical, legal, and ethical concerns for health-care providers as well as family members in regard to how long to sustain life through supportive measures.

See also COMA; CONSCIOUSNESS; END OF LIFE CONCERNS; QUALITY OF LIFE.

poliomyelitis A contagious viral INFECTION, often called simply polio, that affects the nerves and motor function throughout the body. Poliomyelitis is rare today in the United States and other developed countries as a result of aggressive vaccination programs. The first injectable VACCINE to prevent poliomyelitis became available in 1955; a more effective oral vaccine (modified live VIRUS) became available in 1963. The last known "wild" poliomyelitis infection occurred in the United States in 1979. Subsequent poliomyelitis illness resulted from infections acquired in other countries or from exposure of the nonvaccinated to the oral vaccine. The switch to an enhanced inactive (killed) poliovirus vaccine (IPV), capable of providing lifelong immunity, in 1987 eliminated the latter as a cause of poliomyelitis. Oral poliovirus vaccine is no longer available in the United States. Three strains of poliovirus can cause infection. The complete vaccination series consists of four doses of vaccine, one for each strain and a final booster.

Adults who travel to parts of the world where poliomyelitis remains endemic (notably Africa and Southeast Asia) should receive either the complete inactive poliovirus vaccine (IPV) series, if never vaccinated or previous vaccination status is unknown, or an IPV booster otherwise.

Most poliomyelitis is either subclinical (no symptoms) or nonparalytic (runs a course of illness with symptoms similar to those of INFLUENZA). Paralytic poliomyelitis, which affects the BRAIN and SPINAL CORD, occurs in about 2 percent of infections. Among those who develop paralytic poliomyelitis, the risk for death due to PARALYSIS of the muscles of BREATHING and residual paralysis after recovery from the infection are high. More than 90 percent of people who develop nonparalytic poliomyelitis, which affects PERIPHERAL NERVES, recover without complications.

In the late 1970s health experts began tracking the emergence of some polio-like symptoms, such as MUSCLE weakness and generalized fatigue, in

people who had recovered from childhood poliomyelitis. Though researchers do not fully understand what causes postpolio syndrome, it appears to result from damage the poliovirus caused to motor neurons during the active infection rather than a recurrent or new poliomyelitis infection. About one in four people who recover from paralytic poliomyelitis develops postpolio syndrome 10 to 40 years later.

Symptoms and Diagnostic Path

Subclinical poliomyelitis is a very mild infection that does not cause symptoms. The symptoms of nonparalytic poliomyelitis are similar to those of influenza and include

- NAUSEA, VOMITING, and DIARRHEA
- moderate FEVER
- muscle aches and weakness
- extreme fatigue
- irritability
- muscle aches in the lower back and calves
- painful SKIN RASH

The course of nonparalytic illness runs about two weeks, during which symptoms gradually subside. The symptoms of paralytic poliomyelitis are far more severe and are similar to those of MENINGITIS or ENCEPHALITIS. They include

- moderate to high fever
- stiffness and pain in the neck and upper back
- HEADACHE
- rapid onset of muscle weakness that may progress to paralysis within hours
- muscle PAIN and cramping throughout the body
- extreme irritability

The diagnostic path begins with a PERSONAL HEALTH HISTORY to determine the likelihood and circumstances of exposure to the poliovirus. The presence of poliovirus in CEREBROSPINAL FLUID obtained via LUMBAR PUNCTURE confirms the diagnosis.

Treatment Options and Outlook

Treatment is supportive while the infection runs its course, which is typically two to three weeks. Such support may include medications to relieve muscle SPASM and pain, improve gastrointestinal and urinary function, and treat secondary bacterial infections (commonly affecting the urinary tract and the upper respiratory tract). Paralysis that affects breathing may require MECHANICAL VENTILATION.

Most people who survive the course of the disease recover, though many have residual complications such as partial paralysis or muscle deformities that result from the extensive damage to motor neurons. When damage is high in the spinal cord, the person may experience continued difficulty breathing or relatively complete paralysis.

Risk Factors and Preventive Measures

Vaccination prevents infection with the poliovirus; poliomyelitis occurs only in people who have not received proper vaccination or who received vaccination in childhood and travel in later adulthood to parts of the world where poliomyelitis remains endemic (notably Africa and Southeast Asia).

See also INCUBATION PERIOD; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

R

reflex An involuntary response to a stimulus that produces a limited and predictable action. Some reflexes are present only in early infancy and are survival-related, such as the rooting reflex, which guides an infant to locate the nipple for BREASTFEEDING, or the startle (Moro) reflex, in which an infant makes a grasping motion with the arms and legs in response to stimulation that suggests falling. Other reflexes that represent normal neurologic function in infancy may reappear later in life as signs of neurologic damage, such as Babinski's reflex (a spreading of the toes with firm stimulation of the sole of the foot). Reflexes that remain throughout life generally protect the body in some way, such as the gag reflex (which helps prevent large objects from entering the throat) and the corneal reflex (in which contact with the CORNEA causes the eyelid to close). The SPINAL CORD manages most reflexes.

A reflex represents a complete circuit of stimulus, sensory NERVE function, spinal cord (and sometimes BRAIN) participation, and motor nerve function. Neurologists call this circuit a reflex arc. Abnormal reflex responses indicate interruption of the arc and damage to the neurologic structures. A number of reflexes become abnormal when there is TRAUMATIC BRAIN INJURY (TBI) or SPINAL CORD INJURY, for example, or in neurologic disorders that damage brain and nerve tissue such as PARKINSON'S DISEASE and MULTIPLE SCLEROSIS.

See also NEUROLOGIC EXAMINATION.

restless legs syndrome A chronic disturbance of the PERIPHERAL NERVES in the legs that causes symptoms of burning, irritation, itching, crawling sensations, and often PAIN. Accompanying these discomforts is the urge to move the legs, which diminishes the symptoms. Restless legs syndrome is most problematic at night because it interferes with sleep. Neurologists do not know what causes restless legs syndrome, though many believe it is a movement disorder arising from dysfunction of the structures in the midbrain that regulate motor function. Many people receive relief when taking medications used to treat PARKINSON'S DISEASE such as DOPAMINE agonists and levodopa, suggesting disturbances of neurotransmitters such as dopamine and acetylcholine create subtle disruptions of motor response. Restless legs syndrome is also common in people who have Parkinson's disease.

The diagnostic path incorporates a comprehensive NEUROLOGIC EXAMINATION primarily to rule out other potential causes for the symptoms. The neurologist may conduct electromyogram (EMG) studies of the muscles in the legs to evaluate their responses to NERVE impulses. Sleep studies often reveal the extent to which the symptoms interfere with sleep. Treatment may include a combination of medications, such as dopamine agonists, MUSCLE relaxants, sleep aids, and ANALGESIC MEDICATIONS for pain relief. Some people experience relief from symptoms and improved sleep with alternative therapies such as ACUPUNCTURE and BIOFEEDBACK.

Restless legs syndrome affects 12 to 20 million Americans. Many people who have restless legs syndrome do not seek medical care because they do not know there are treatments available to ease their symptoms. Restless legs syndrome is chronic, often developing in midlife or later. There are no known measures to prevent restless legs syndrome.

See also APNEA; NEUROTRANSMITTER; SLEEP DISORDERS.

Reye's syndrome A rare complication of certain viral infections in children, notably CHICKENPOX,

upper respiratory INFECTION, and INFLUENZA (the flu). Researchers do not know what causes Reye's syndrome to develop though it is significantly more likely to occur in children who receive aspirin or bismuth subsalicylate (Pepto Bismol) to treat the symptoms of their viral infections.

There is a strong correlation between aspirin and other salicylates (such as bismuth subsalicylate, better known as the trade product Pepto Bismol) and Reye's syndrome in children. Do *not* give these products to children who may have viral infections.

Though Reye's syndrome affects multiple organ systems, the most serious consequence (and usually the first indication of the syndrome's appearance) is ENCEPHALOPATHY (disturbances of BRAIN function). Early diagnosis and aggressive therapeutic intervention are essential to prevent or manage metabolic and neurologic complications. Reye's syndrome can be fatal.

Symptoms and Diagnostic Path

The first symptoms of Reye's syndrome are those of encephalopathy developing within a week of a viral infection. These symptoms include

- confusion
- memory disturbances
- agitation
- progressive UNCONSCIOUSNESS

Reye's syndrome causes excessive deposits of fatty acids in the LIVER; thus liver biopsy provides the definitive diagnosis. The deposits interfere with the liver's ability to function, resulting in systemic metabolic disturbances, such as electrolyte and enzyme imbalances, that are apparent from BLOOD tests. Deposits of fatty acids may accumulate in other organs as well, such as the HEART, KIDNEYS, and PANCREAS.

Treatment Options and Outlook

A child who has Reye's syndrome requires hospitalization in the intensive care unit. Because the cause of Reye's syndrome remains unknown, treatment is supportive and aims to manage the constellation of metabolic disturbances that typify the syndrome. These metabolic disturbances often cause serious complications such as ARRHYTHMIA (abnormal electrical activity in the heart) and HYPOTENSION (low BLOOD PRESSURE). Kidney function also may suffer, leading to RENAL FAILURE.

Overall about 75 percent of children survive Reye's syndrome; about two thirds of survivors have no long-term consequences. When such consequences occur, they may include SEIZURE DISORDERS, intellectual impairment, and neuromuscular dysfunction. The later the stage of Reye's syndrome at the time of diagnosis, the higher the risk for complications, including death.

Risk Factors and Preventive Measures

Reye's syndrome occurs nearly exclusively in children under age 15 years and develops during the course of a viral infection. IMMUNIZATION for influenza and chickenpox can prevent these infections, which are commonly associated with Reye's syndrome. There are no known measures for preventing Reye's syndrome. Early diagnosis and aggressive treatment are essential for optimal recovery.

See also CHILDHOOD DISEASES.

rhizotomy A surgical OPERATION to selectively sever segments (rootlets) of the dorsal (back) or ventral (front) roots of a spinal NERVE to treat intractable and debilitating PAIN or spasticity such as may occur with neuromuscular disorders. The operation reduces the number of nerve impulses the nerve roots convey. Rhizotomy may be an appropriate treatment for CEREBRAL PALSY, SPINAL CORD INJURY, and other conditions that generate DYSTONIA, CHOREA, or ATHETOSIS. Rhizotomy generally becomes a therapeutic option only when other methods have failed to control symptoms, though may be an earlier recommendation for certain presentations of spastic cerebral palsy. The neurosurgeon performs the operation with the person under general ANESTHESIA. Risks and complications of rhizotomy include excessive bleeding, postoperative INFECTION, altered sensory perception in the affected limb (usually foot or leg), and, rarely, PARALYSIS.

See also BOTULINUM THERAPY; SURGERY BENEFIT AND RISK ASSESSMENT.

S

seizure disorders Abnormal discharge of electrical activity in certain areas of the BRAIN that causes various involuntary consequences. Most seizures originate in areas of the cerebral cortex.

Seizure disorders may occur spontaneously (without identifiable cause) or as a consequence of damage to the brain such as TRAUMATIC BRAIN INJURY (TBI) or CEREBRAL PALSY. Among the more common forms of seizure disorders are

- epilepsy, in which seizures are recurrent and often frequent
- absence seizures, in which the person experiences very brief episodes of loss of consciousness though often is unaware they occur
- clonic–tonic seizures, in which the person loses consciousness and there is convulsive movement of the legs and arms
- focal seizures, in which the person may or may not lose consciousness and the seizure affects a specific and localized part of the body

Seizures generally end within a minute and do not themselves harm injuries may occur if a person falls or has a seizure in a hazardous location such as a swimming pool. There is no reason to intervene with a person who is having a seizure, other than for safety. Some people, especially children, may have seizures during FEVER. Such seizures, called febrile seizures, do not indicate the person has a seizure disorder.

Symptoms and Diagnostic Path

Seizure disorders run the gamut from causing barely noticeable to disabling symptoms. The diagnostic path includes a thorough PERSONAL HEALTH HISTORY, NEUROLOGIC EXAMINATION, ELECTROENCEPHALOGRAM (EEG), and diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI). The EEG typically shows irregularities in electrical activity even when the person is not having seizures. Because sleep deprivation makes the brain more sensitive to electrical activity, the neurologist may request the person remain awake for 24 hours before the EEG. These procedures are generally conclusive for diagnosing seizure disorders.

Treatment Options and Outlook

Antiseizure medications are the mainstay of treatment for seizure disorders. Often a person may require two or more medications that have different actions to adequately suppress inappropriate electrical activity in the brain and prevent seizures from occurring. Because antiseizure medications alter the brain's biochemistry and have potentially serious side effects, neurologists tend not to treat a single episode of seizure but opt instead to take an approach of watchful waiting.

MEDICATIONS TO TREAT SEIZURE DISORDERS

carbamazepine (Tegretol)	gabapentin (Neurontin)
lamotrigine (Lamictal)	levetiracetam (Keppra)
oxcarbazepine (Trileptal)	phenobarbital
phenytoin (Dilantin)	tiagabine (Gabitril)
topiramate (Topamax)	valproic acid (Depakote)
zonisamide (Zonegran)	

Treatment is generally long-term, though children may outgrow certain kinds of seizure disorders. Medications successfully prevent seizures in most people, though require regular monitoring to ensure that BLOOD concentrations remain therapeutic. Dysfunctions of the LIVER and KIDNEYS are the most significant side effects of antiseizure

medications. Surgery to interrupt electrical activity in the brain is sometimes an option for intractable seizures (seizures that fail to respond to medication therapy).

Risk Factors and Preventive Measures

Neurologists do not know the cause of most seizure disorders; thus there are no measures known to prevent them from developing. People who have recurrent seizures or do not experience full suppression of seizures with treatment should not drive or engage in other activities that can put them or others at risk. Many states have laws that regulate the conditions under which a person who has a seizure disorder may obtain a driver's license; such laws vary among states.

See also MYOCLONUS.

spina bifida A form of neural tube defect in which the distal (lower) portion of the neural tube fails to close early in embryonic development. In very mild spina bifida the defect may be unapparent and cause no problems. Severe spina bifida leaves the SPINAL CORD partially or completely exposed, resulting in numerous complications that often include deformity and PARALYSIS. Doctors identify three forms of spina bifida:

- Spina bifida occulta is the most common and the mildest form. Only a small portion of a single vertebra fails to close properly. The spinal cord and the SPINAL NERVES develop correctly. The surface of the spine looks and feels normal, and the person has no symptoms.
- Meningocele is when the meninges (membranes that enclose the spinal cord) protrude under the surface of the SKIN through the incompletely closed vertebrae (usually two or more). The spinal cord and spinal nerves develop correctly, however.
- Myelomeningocele is the most severe form. The spinal canal is open and exposed along the lower spine. The spinal cord and meninges typically appear as a saclike structure, which may be under or on top of the skin. The spinal cord and spinal nerves do not develop correctly, and often there are deformities of the pelvis, abdominal and pelvic organs, and lower limbs.

Meningocele and myelomeningocele are rare. Myelomeningocele can be life threatening, depending on its location and the extent of exposure of the spinal cord, which presents a significant risk for INFECTION (MENINGITIS or ENCEPHALITIS).

Symptoms and Diagnostic Path

Diagnostic prenatal ULTRASOUND detects many neural tube defects before birth. At birth, symptoms of meningocele and myelomeningocele are apparent as deformities of the spine. COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) help the neurosurgeon assess the extent of the damage and plan an appropriate course of treatment.

Treatment Options and Outlook

Spina bifida occulta requires no treatment. Surgery is necessary to repair meningocele, though nearly always recovery is complete. Meningocele repair often heals with minimal or no residual consequences, and the child grows up with normal neurologic function. Complex surgery often is necessary to repair myelomeningocele, and residual complications are usually extensive. Ongoing complications include paralysis, deformity, and HYDROCEPHALY (excessive CEREBROSPINAL FLUID) that requires a shunt. Children born with myelomeningocele require lifetime medical and supportive care. Many have permanent URINARY INCONTINENCE and FECAL INCONTINENCE because the lower spinal cord, which is nonfunctional, regulates urination and defecation. Some may learn to walk with crutches or braces. Developmental delays and LEARNING DISORDERS are common.

Risk Factors and Preventive Measures

Folic acid supplementation greatly reduces the risk for neural tube defects such as spina bifida, perhaps by 70 percent. Health experts recommend that all women of childbearing ability and age take daily folic acid supplement regardless of their pregnancy plans, as the most important period of supplementation appears to be the four to six weeks before CONCEPTION through the first trimester of pregnancy. Some antiseizure medications (notably valproic acid), DIABETES, and OBESITY increase the risk for neural tube defects. Though most spina bifida seems to occur spontaneously,

women who have had one child with spina bifida are more likely to have others. Researchers are not certain whether the connection is genetic or environmental.

See also BIRTH DEFECTS; NEURAL TUBE DEFECTS; PRENATAL CARE.

spinal cord The largest NERVE in the body, extending from the base of the BRAIN (medulla oblongata) through the spinal canal to the second lumbar vertebra. The average adult spinal cord is 16 to 20 inches long and about the thickness of a man's thumb. The outer structure of the spinal cord is white matter (myelinated neuronal axons); the inner structure is gray matter (NEURON cell bodies). The inner gray matter is roughly the shape of an H, with the horns extending to the roots of the 31 pairs of SPINAL NERVES that branch from the spinal cord.

The spinal cord is the primary neurologic conduit between the body and the brain. It transmits motor nerve impulses from the brain to the body and sensory nerve impulses from the body to the brain. The spinal cord also has rudimentary filtering and control functions, responding to certain kinds of nerve impulses, and serves as the center for reflexes related to urination, defecation, and MUSCLE stretch (essential for movement and balance).

The spinal column, a sequence of joined vertebrae, encloses and protects the spinal cord. CARTILAGE cushions between each vertebra (vertebral disks) allow the spine to flex and twist without jeopardizing the spinal cord. Significant trauma, such as may occur in an automobile accident, can compress, bruise, or sever the spinal cord. Such injuries cause paralysis. A severed spinal cord cannot regenerate, though sometimes partial to full function returns with release of the source of compression or after HEALING of a bruise. Tumors may also compress the spinal cord.

For further discussion of the spinal cord within the context of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also HERNIATED NUCLEUS PULPOSUS; MOTOR VEHICLE ACCIDENTS; NEUROFIBROMATOSIS; REFLEX; SPINAL CORD INJURY.

spinal cord injury Traumatic damage to the SPINAL CORD, usually the result of a blow to the spine or sudden, forceful twisting. MOTOR VEHICLE ACCIDENTS account for 40 percent and VIOLENCE (gunshot and knife wounds) accounts for 25 percent of spinal cord injuries in the United States. Other common causes are diving into shallow water, sports-related injuries, and significant falls. More than 80 percent of those who experience spinal cord injuries are men, more than half of whom are under age 30.

SPINAL CORD injury is a medical emergency that requires immediate treatment at a neurologic trauma center. It is critical that only properly trained medical personnel attempt to move someone who may have suffered a spinal cord injury.

Such injuries typically cause the vertebrae to compress the spinal cord, damaging the long axons that make up the spinal cord's white matter. The axons are the fibers that extend from neurons in the BRAIN and brainstem. This type of injury, which neurologists classify as incomplete, permits some NERVE impulses to travel the spinal cord and is sometimes recoverable. Much less commonly, trauma partially or completely severs the spinal cord. A complete spinal cord injury exists when no nerve impulses can travel through or around the point of trauma. Circumstances that increase the damage include bleeding, which can increase pressure and/or directly damage neurons, and a surge of neurotransmitters, notably glutamate, at the site of the injury, which overwhelms and kills neurons.

Symptoms and Diagnostic Path

The primary symptom of spinal cord injury is immediate PARALYSIS below the point of trauma. When the injury is high on the spinal cord, above the lumbar vertebrae, the paralysis may affect the DIAPHRAGM and muscles of the chest, preventing the mechanics of BREATHING from taking place. Injury at the cervical level is most severe; injury at the C1 or C2 level is usually not survivable because this is the level of neurologic functions

that support survival such as respiration, BLOOD PRESSURE, and HEART RATE. COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) can show the full extent of the injury.

Treatment Options and Outlook

The standard of care is to administer an intravenous corticosteroid medication, methylprednisolone, within eight hours of a spinal cord. The methylprednisolone reduces the body's natural inflammatory response, lessening the risk for added pressure within the spinal canal and the direct damage to neurons that INFLAMMATION causes. Other treatment options may include surgery to stabilize the spine and remove any BONE fragments or debris from the spinal canal or using braces to immobilize the spine. Supportive measures such as MECHANICAL VENTILATION may be necessary, depending on the level of the injury.

Ongoing treatment typically includes early and aggressive PHYSICAL THERAPY, OCCUPATIONAL THERAPY, and other rehabilitation approaches to maintain MUSCLE tone and STRENGTH as well as to restore as much independence as possible. Much of this treatment may take place at an inpatient rehabilitation center that specializes in spinal cord injuries. Many people are able to recover to a reasonable level of function through the use of mobility aids and assistive devices. When the injury is incomplete, full recovery is sometimes possible. However, it is difficult for neurologists to predict what level of recovery is likely. An individual's general health condition, motivation, and persistence are important influences.

Risk Factors and Preventive Measures

Measures that reduce the risks for spinal cord injury are those that lower the likelihood of motor vehicle accidents. Many of these risks are behaviors such as excessive speed, driving while intoxicated, and failure to wear seat belts. Proper technique and equipment for athletic activities such as horseback riding, downhill skiing, bicycling, and contact sports help improve the safety of participating in these events.

See also CORTICOSTEROID MEDICATIONS; NEURON; NEUROTRANSMITTER; QUALITY OF LIFE; TRAUMATIC BRAIN INJURY (TBI).

spinal nerves The 31 paired nerves that branch from the SPINAL CORD, extending into the body to form the PERIPHERAL NERVES. The spinal nerves and the CRANIAL NERVES together make up the PERIPHERAL NERVOUS SYSTEM. The spinal nerves emerge from the gray matter of the spinal cord in two roots. The ventral (anterior or front) spinal NERVE root is the motor portion of the spinal nerve that carries nerve impulses from the BRAIN and spinal cord to the peripheral body. The dorsal (posterior or back) spinal nerve root is the sensory portion of the spinal nerve that carries nerve impulses from the body to the spinal cord and brain. Each spinal nerve root immediately branches into several rootlets, which subsequently give rise to the peripheral nerves that serve the body (excluding the head and face).

SPINAL NERVE PAIRS

cervical: 8 pairs, designated C1 through C8
thoracic: 12 pairs, designated T1 through T12
lumbar: 5 pairs, designated L1 through L5
sacral: 5 pairs, designated S1 through S5
coccygeal: 1 pair, designated CO1

Spinal nerve pairs C1 through C4 serve the neck and are collectively referred to as the cervical plexus. Spinal nerve pairs C5 through T1 serve the upper extremities and main trunk and are collectively known as the thoracic plexus. Spinal nerve pairs L1 through L5 (the dorsal roots of L4 and L5) serve the lower back and legs and are collectively referred to as the lumbar plexus. Spinal nerve pairs L4 (the ventral roots of L4 and L5) through S3 serve the structures of the lower abdomen and are collectively known as the sacral plexus. Spinal nerve pairs S4, S5, and CO1 serve the structures of the pelvis, including the genitals, and are collectively known as the pudendal plexus.

For further discussion of the spinal nerves within the context of the structures and functions of the nervous system, please see the overview section "The Nervous System."

See also MULTIPLE SCLEROSIS; SPINA BIFIDA; SPINAL CORD INJURY.

stupor A state in which a person is unaware of and does not interact with the external environ-

ment except when vigorously stimulated to brief arousal. Stupor is very near COMA on the scale of CONSCIOUSNESS. Stupor may result from numerous circumstances, including HYPOGLYCEMIA (low BLOOD GLUCOSE level), INTOXICATION, HYPOXIA (lack of oxygen), injury (TRAUMATIC BRAIN INJURY [TBI] or CONCUSSION), ENCEPHALOPATHY, seizures, DRUG overdose, and poisoning. Because some causes of stupor are potentially lethal, doctors attempt to identify them quickly. Treatment depends on underlying cause.

See also PERSISTENT VEGETATIVE STATE; SEIZURE DISORDERS; UNCONSCIOUSNESS.

T–U

tardive dyskinesia See DYSKINESIA.

thalamotomy A surgical procedure in which the neurosurgeon destroys a small portion of the THALAMUS, which plays a role in certain kinds of motor movement. Thalamotomy may be an appropriate treatment for tremor-predominant PARKINSON'S DISEASE, tremor disorders such as benign essential tremor, and DYSTONIA. Neurosurgeons first performed thalamotomy in the 1950s. Until recent advances in technology, however, the risks of the surgery (especially damage to adjacent BRAIN structures) were far greater than the benefits. Current neurosurgery techniques use MAGNETIC RESONANCE IMAGING (MRI) to locate the portions of the thalamus that participate in movement, typically the ventral intermediate (VIM) nucleus. The neurosurgeon then uses MRI to precisely guide the insertion and placement of a thin probe into the VIM. A burst of heat through the electrode ablates, or destroys, a few cells at a time until the OPERATION achieves the desired result. The person remains conscious during the operation and responds with movements as the neurosurgeon directs.

The first step of thalamotomy is the placement of a stereotactic halo, a circular brace the neurosurgeon attaches to the skull (done under local anesthetic). The halo holds the instruments steady and in precise position during the operation. The neurosurgeon uses a local anesthetic to numb the SKIN and periosteum covering the cranium, the only areas that contain nerves sensitive to PAIN, and drills a small hole in the BONE. The neurosurgeon slowly feeds the probe toward the thalamus, using MRI to guide the process. The operation takes 60 to 90 minutes, and improvement is apparent immediately. The neurosurgeon removes the stereotactic halo when the operation is completed. Complications are rare; when they do occur they may include excessive bleeding, postoperative INFECTION, and stimulation of taste or visual disturbances (due to the probe passing near or through these areas of the brain). Most people return to full and regular activities in about two weeks.

The effects of thalamotomy are permanent and may end symptoms for some people, especially those who have benign essential tremor. Symptoms often reemerge when the underlying condition is progressive. However, thalamotomy is not very effective treatment for the DYSKINESIA of classic Parkinson's disease.

See also DEEP BRAIN STIMULATION; PALLIDOTOMY; SURGERY BENEFIT AND RISK ASSESSMENT.

tic An involuntary MUSCLE SPASM that typically occurs repetitiously and spontaneously. Tics most commonly involve muscle groups in the face and neck and may appear purposeful, such as an eyelid tic that gives the appearance of winking or a tic involving the muscles around the MOUTH that causes a person to look as though he or she were grimacing. Vocal tics are spasms that involve the VOCAL CORDS and produce noises such as grunts. Tics are very common, especially in childhood, and in isolation usually have no neurologic significance. Some people experience tics during times of anxiety. Tics that persist or occur in conjunction with other symptoms may indicate a compressed NERVE or an underlying neurologic or neuromuscular condition. Tic disorders that reflect neurologic disturbances include TOURETTE'S SYNDROME and tic douloureux (more commonly called trigeminal NEURALGIA).

See also CEREBRAL PALSY; DYSKINESIA.

Tourette's syndrome A neurologic disorder in which a person experiences an array of tics (involuntary and repetitive movements). Researchers believe Tourette's syndrome results from subtle imbalances of neurotransmitters in the BRAIN. The imbalances cause disturbances of motor function that affect the muscles of movement as well as functions of articulation and vocalization. Most people who have Tourette's syndrome experience simple neuromuscular tics such as involuntary movements of the eyelids or MOUTH, or even the head and extremities. Some people also experience vocal tics, in which they express noises such as grunts and coughs. And some people experience articulation tics in which they speak words, sometimes obscenities, involuntarily and often loudly, as though the words erupted from them. Although these tics have the appearance of conscious behavior (and some people can temporarily suppress them through conscious effort), they are involuntary neurologic disturbances.

There are no clear diagnostic markers for Tourette's syndrome. Symptoms typically begin in childhood, around age seven or eight, and peak during ADOLESCENCE before trailing off. Many people who have Tourette's syndrome have few episodes of tics after they reach midlife, though neurologists consider Tourette's syndrome a chronic, lifelong condition. When evaluating the symptoms of Tourette's syndrome, the neurologist may conduct numerous tests and procedures to rule out other potential causes, including psychiatric illness, of the symptoms. The neurologist will generally make the diagnosis of Tourette's syndrome after ruling out such possibilities and when symptoms persist for a year or longer.

Many people who have Tourette's syndrome respond to combinations of medications including ANTIPSYCHOTIC MEDICATIONS, ANTIDEPRESSANT MEDICATIONS, STIMULANTS, and the BLOOD PRESSURE medication clonidine (Catapres). All of these medications have varied effects on neurotransmitters and the brain's biochemical balance. Though it may take a period of trial and error to find the combination that is most effective for each individual, nearly everyone who has Tourette's syndrome experiences diminished symptoms with appropriate treatment. Though the tics, especially the vocalizations and articulations, can be disconcerting, Tourette's syndrome does not result from significant neurologic damage and does not threaten health or well-being. SUPPORT GROUPS and therapists can help people develop COPING MECHANISMS for living with Tourette's syndrome. Because stress and anxiety exacerbate symptoms, people who have Tourette's syndrome generally benefit from stress reduction methods and approaches such as BIOFEEDBACK.

See also ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD); NEUROTRANSMITTER; OBSESSIVE–COMPULSIVE DISORDER (OCD); STRESS AND STRESS MANAGEMENT; TIC.

traumatic brain injury (TBI) Damage, often permanent, to the BRAIN that results from trauma, blunt or open. TBI may be acute (occur suddenly) or chronic (occur over time as a result of cumulative injuries). Acute TBI most often occurs from a blow to the head, such as from a significant fall or collision. Open trauma to the head, such as gunshot wound, may also result in acute TBI. Chronic TBI develops in people who receive repeated blows to the head, such as athletes who participate in contact or collision sports. Boxing, soccer, and American football are the leading causes of chronic TBI in the United States. The effects of TBI may range from mild disturbances of thought or movement to incapacitating loss of cognitive and motor function or PERSISTENT VEGETATIVE STATE.

Shaken baby syndrome, a form of CHILD ABUSE, is a significant and preventable cause of TRAUMATIC BRAIN INJURY (TBI) in young children. Children are especially vulnerable to brain injury and may experience permanent damage or die from events that would not harm an adult.

Symptoms and Diagnostic Path

Symptoms of TBI may be vague and mild or sudden and severe. Common symptoms include

- significant or persistent HEADACHE
- loss of CONSCIOUSNESS
- unequal dilation of the pupils
- weakness or PARALYSIS on one side of the body
- blurred or double vision (DIPLOPIA)

- ringing in the ears (TINNITUS)
- progressive loss of cognitive function and memory
- seizures
- personality changes

The diagnostic path begins with an assessment of any history of trauma to the head, such as falls or MOTOR VEHICLE ACCIDENTS. When a single event is not apparent, the doctor will look for cumulative injury. A NEUROLOGIC EXAMINATION can identify signs of sensory or motor disturbances that suggest the areas of the brain where there may be injury. Diagnostic imaging procedures, such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI), often reveal signs of injury such as subdural or intracranial HEMATOMA, cranial FRACTURE, or altered brain structure. ELECTROENCEPHALOGRAM (EEG) may provide further evidence in the form of abnormal electrical activity in certain areas of the brain.

Treatment Options and Outlook

Treatment depends on the cause and extent of the injury. Surgery is often necessary to drain collected BLOOD (hematoma), relieve pressure, remove BONE fragments or other matter when there is an open wound, or repair damaged blood vessels. Most treatment targets maintaining and restoring brain function through PHYSICAL THERAPY, OCCUPATIONAL THERAPY, and speech therapy. A person may need to relearn basic activities of daily living, or to use his or her nondominant hand. Rehabilitation may also target lost abilities such as reading or writing. The extent of recovery depends on the nature of the injury and the person's overall health status and age. Though traumatic brain injury typically results in some degree of permanent symptoms, many people are able to recover enough to return to an acceptable level of independent living.

Significant injury may result in COMA (UNCONSCIOUSNESS that extends for a few hours to a month) or persistent vegetative state (unconsciousness that persists beyond a month). Though CT scan or MRI can help the neurologist monitor the state of physical damage within the brain, it is difficult to project the likelihood for recovery. A person can remain in a persistent vegetative state for months to years.

Risk Factors and Preventive Measures

Blows to the head are the primary risk factor for traumatic brain injury. Preventive measures include wearing seat belts, helmets, and other protective equipment. Appropriate training and methods reduce the risk for head injuries that occur during sporting events and competitive athletics.

See also COGNITIVE FUNCTION AND DYSFUNCTION; MEMORY AND MEMORY IMPAIRMENT; SEIZURE DISORDERS; STROKE.

tremor disorders Conditions in which there is damage to the areas of the BRAIN that regulate or coordinate movement, resulting in involuntary, rhythmic back-and-forth movements of the extremities (most commonly the hands) and sometimes the head. Such damage may result from STROKE; injury; or, some researchers speculate, the cumulative effect of NEURON loss over the course of the lifetime. Tremor disorders become increasingly common with advancing age. The most common tremor disorder is benign essential tremor, which affects about five million Americans most of whom are age 60 or older.

BENIGN ESSENTIAL TREMOR VERSUS PARKINSON'S DISEASE

Though tremor is a symptom of PARKINSON'S DISEASE, Parkinson's disease is not a tremor disorder and tremor disorders do not indicate a person has Parkinson's disease. The tremors that characterize Parkinson's disease are most intense when the hands are still and diminish with activity. Tremors of benign essential tremor are most intense during activity and may entirely disappear when the affected limbs are at rest.

Symptoms and Diagnostic Path

Tremors tend to develop gradually and may worsen during times of stress or anxiety. They first appear as mild and intermittent trembling. Over time the movement becomes more clearly rhythmic and begins to interfere with tasks such as holding a pen to write. Tremors may also affect the VOCAL CORDS, making the voice sound wavering. This is the point at which people tend to seek

medical care. The diagnostic path begins with a complete PERSONAL HEALTH HISTORY and family health history. The neurologist conducts a NEUROLOGIC EXAMINATION, and may conduct COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) of the brain to look for changes that suggest other causes for the tremors. The diagnosis combines the neurologist's clinical observations about the characteristics of the tremor with negative findings for other causes.

Treatment Options and Outlook

Medications to mitigate tremors include beta blockers such as propanolol, certain ANTISEIZURE MEDICATIONS (notably primidone), and MUSCLE relaxants such as alprazolam. BOTULINUM THERAPY, in which the neurologist injects botulinum toxin into affected muscles to paralyze them, can provide long-term relief for some people. Surgical interventions such as DEEP BRAIN STIMULATION and THALAMOTOMY may be options for tremors that fail to respond to less invasive treatments. Most people are able to find treatments that minimize the extent to which tremors interfere with their daily activities.

Risk Factors and Preventive Measures

Benign essential tremor appears to run in families. About half of tremor disorders appear to occur in people who mutations in one or both of two genes, *etm1* and *etm2*. Researchers suspect as yet unidentified mutations in other genes are responsible for tremor disorders in people who do not have *etm1* or *etm2* mutations. Other tremor disorders may have genetic components as well. Tremor disorders are far more common in people who are older than age 60 than in those who are younger. However, there are no known measures to prevent tremor disorders.

See also DYSKINESIA; GENE; MUTATION; PARESTHESIA.

unconsciousness A state in which a person is unaware of and does not interact with the external environment. The most common experiences of unconsciousness are sleep, fainting (SYNCOPE), and general ANESTHESIA. Unconsciousness may also occur with CONCUSSION, seizures, HYPOTENSION (low BLOOD PRESSURE), ENCEPHALITIS, ENCEPHALOPATHY, and INTOXICATION. Most people are easily aroused from the unconsciousness of sleep though people who are unconsciousness due to other causes may not arouse until or if the underlying cause resolves.

See also ARRHYTHMIA; BRAIN DEATH; CONSCIOUSNESS; COMA; LONG QT SYNDROME (LQTS); PAROXYSMAL ATRIAL TACHYCARDIA (PAT); PERSISTENT VEGETATIVE STATE; SEIZURE DISORDERS; WOLFF-PARKINSON-WHITE SYNDROME.

THE MUSCULOSKELETAL SYSTEM

The musculoskeletal system encompasses the bones, muscles, tendons, ligaments, and fasciae. Practitioners who diagnose and treat health conditions of the musculoskeletal system are orthopedists (also called orthopedic surgeons). Orthopedists may further specialize in sports medicine or physiatry (rehabilitative medicine).

This section, "The Musculoskeletal System," present a discussion of the structure and function of the bones, muscles, and other connective tissues. It also contains entries about the health conditions that can affect musculoskeletal function.The section "The Nervous System" contains entries for conditions that affect musculoskeletal function but are primarily neurologic in nature.

Structures of the Musculoskeletal System

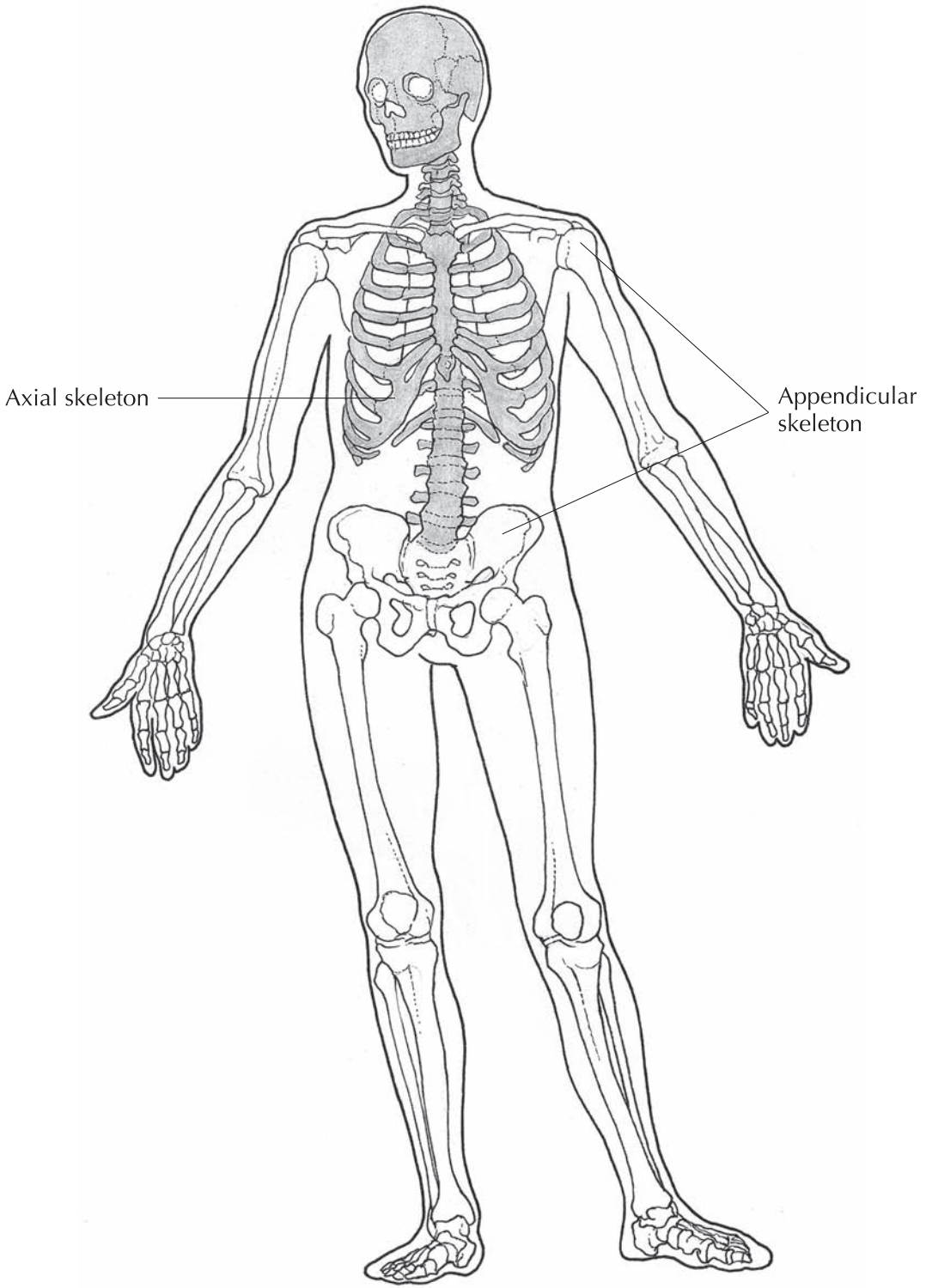
Bones

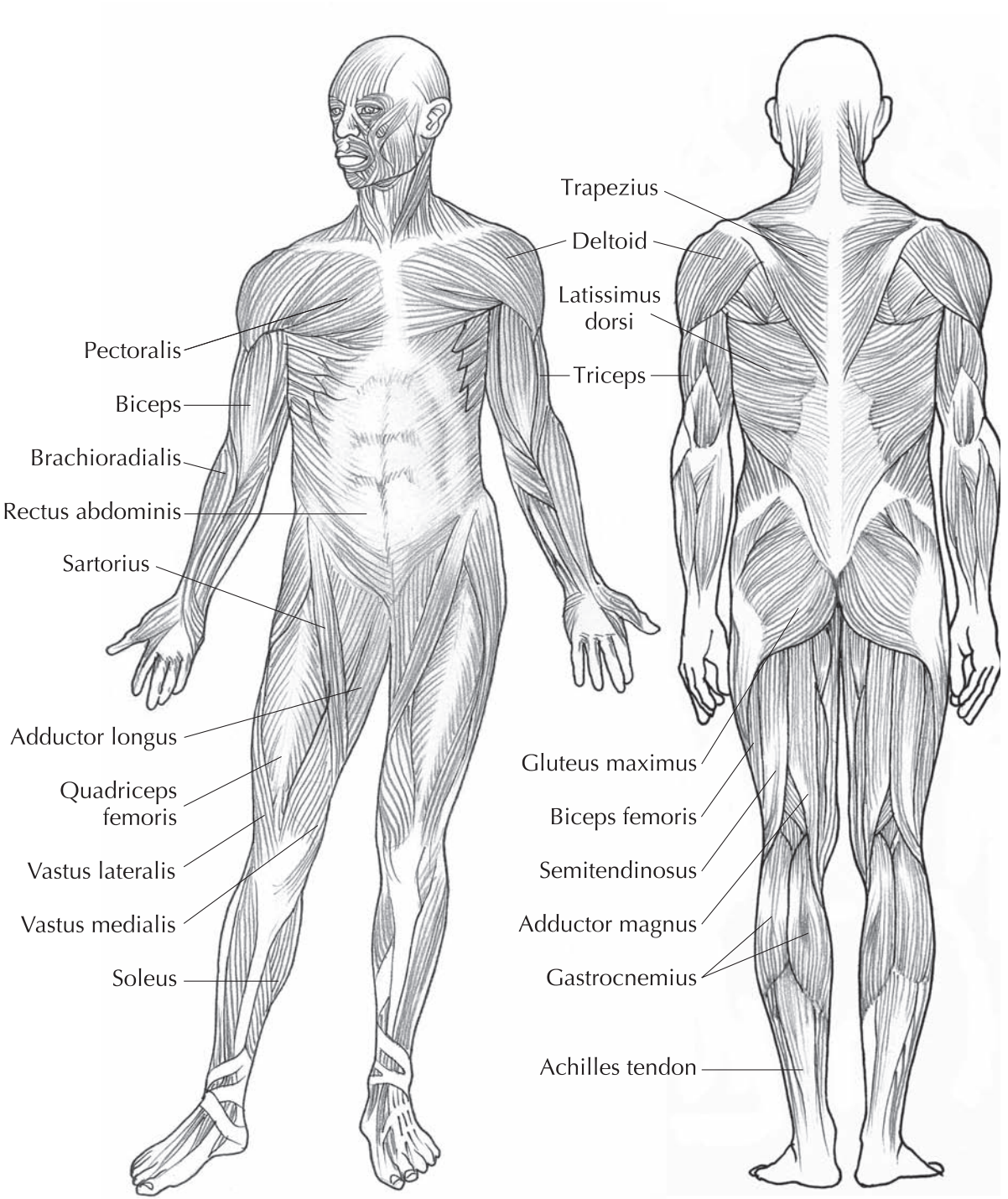
axial SKELETON: 80 bones
- head (cranium): 8
  - frontal 2
  - parietal 1
  - temporal 2
  - occipital 1
  - ethmoid 1
  - sphenoid 1
- auditory ossicles: 6
  - malleus 1 each ear
  - incus 1 each ear
  - stapes 1 each ear
- face: 14
  - lacrimal 2
  - nasal 2
  - zygoma 2
  - turbinate 2
  - vomer 1
  - maxilla 2
  - palate 2
  - mandible 1
- hyoid: 1
- spine: 26
  - ervical vertebrae 7
  - thoracic vertebrae 12
  - lumbar vertebrae 5
  - sacrum 1
  - coccyx 1
- sternum: 1
- ribs: 24
  - 12 pairs each side

appendicular skeleton: 120 bones
- clavicle (collarbone): 2
- scapula (shoulder blade): 2
- upper arm: 2
  - humerus 1 each arm
- lower arm: 4
  - radius 1 each arm
  - ulna 1 each arm
- carpal (wrist): 16
  - scaphoid 1 each wrist
  - lunate 1 each wrist
  - triquetrum 1 each wrist
  - pisiform 1 each wrist
  - trapezium 1 each wrist
  - trapezoid 1 each wrist
  - capitate 1 each wrist
  - hamate 1 each wrist
- metacarpal (hand): 10
  - 5 each hand
- phalanx (finger): 28
  - 14 each hand
- innominate (pelvis): 2
  - fusion of ilium, ischium, pubis 1 each side
- upper leg: 2
  - femur 1 each leg
- patella (kneecap): 2
  - 1 each leg
- lower leg: 4
  - fibula 1 each leg
  - tibia 1 each leg
- tarsal (ankle): 14
  - talus 1 each ankle
  - calcaneus 1 each ankle
  - navicular 1 each ankle
  - cuboid 1 each ankle
  - cuneiform 3 each ankle
- metatarsal (foot): 10
  - 5 each foot
- phalanx (toe): 28
  - 14 each foot
- TEETH (permanent): 32
  - incisor 4 top, 4 bottom, front center of mouth
  - cuspid 2 top, 2 bottom, each side of mouth
  - bicuspid 4 top, 4 bottom, in pairs on each side of MOUTH
  - molar 6 top, 6 bottom, 3 at the back of each side of mouth

Major Skeletal Muscles

- head, neck, and shoulders
  - frontalis
  - orbicularis oculi
  - masseter
  - temporalis
  - medial pterygoid
  - trapezius
  - semispinalis capitis
  - splenis capitis
  - sternocleidomastoid
- arm
  - deltoid
  - biceps
  - triceps
  - brachialis
  - brachioradialis
  - palmaris longus
  - extensor carpi radialis
  - flexor carpi radialis
  - extensor carpi ulnaris
  - flexor carpi radialis
  - extensor digitorum
  - lexor digitorum
  - abductor pollicis brevis
  - abductor pollicis longus


Axial skeleton
Appendicular skeleton


Pectoralis
Biceps
Brachioradialis
Rectus abdominis
Sartorius
Adductor longus
Quadriceps femoris
Vastus lateralis
Vastus medialis
Soleus
Trapezius
Deltoid
Latissimus dorsi
Triceps
Gluteus maximus
Biceps femoris
Semitendinosus
Adductor magnus
Gastrocnemius
Achilles tendon

- torso
  - pectoralis major
  - pectoralis minor
  - serratus anterior
  - external oblique
  - internal oblique
  - intercostal
  - diaphragm
  - transverse abdominus
  - rectus abdominis
  - iliopsoas
- back
  - teres major
  - infraspinatus
  - rhomboideus major
  - latissimus dorsi
  - gluteus maximus
  - gluteus medius
  - obturator
- leg
  - pectineus
  - sartorius
  - adductor longus
  - rectus femoris
  - adductor magnus
  - gracilis
  - biceps femoris
  - semitendinosus
  - vastus lateralis
  - vastus medialis
  - semimembranosus
  - tibialis anterior
  - tibialis posterior
  - gastrocnemius
  - soleus
  - peroneus longus
  - flexor hallucis
  - extensor

Functions of the Musculoskeletal System

The musculoskeletal system gives the body form and structure, protects the internal organs, and provides movement. It determines body height and mass. It is the foundation for facial features, hand characteristics, and athletic ability. The bones of the SKELETON form the core of the structural body; the muscles build the body's outward appearance. In tandem, the bones and the muscles carry the body through life.

A soft start: the skeleton's origins The SKELETON arises from the mesoderm very early in embryonic development, taking rudimentary form at about three weeks of gestational age. Hyaline CARTILAGE, a tough, dense type of connective tissue, forms the template that will become the ossified (mineral-hardened) skeleton. Though the process of ossification begins before birth, the greater percentage of the skeleton is still cartilage at birth to facilitate passage through the birth canal.

After birth an intricate, HORMONE-regulated process immediately sets about to convert cartilage cells (chondrocytes) to BONE cells (osteocytes). This process of ossification takes the first two decades of life to reach fruition. Bone tissue continues to grow and change throughout life even after bone size reaches stability through another process called bone remodeling, in which bone-building cells (osteoblasts) create new bone structure in synchronization with bone-destroying cells (osteoclasts) which remove old bone structure.

Framework: the skeleton The 206 bones of the adult human skeleton give the body shape, protection, and mobility. There are two divisions of the skeleton:

- The axial skeleton forms the body's central alignment; its bones are primarily those of support and shelter.
- The appendicular skeleton "hangs from" the axial skeleton; its bones are primarily those of movement.

Bones provide the structure that gives the body resistance against gravity and makes movement possible. Long bones, such as those in the arms and legs, function as levers for the skeletal muscles to generate movement and locomotion. A honeycombed structure within the long bones reduces their density and weight while increasing their STRENGTH. The compact construction of short bones, such as those in the hands and feet, supports functions that require greater strength and less leverage. Flat bones, such as the scapulae (shoulder blades) and pelvis (hip bones), provide surface area for firmly anchoring the large skeletal muscles that make movement possible.

Some bones function as armor, protecting vital structures and organs. The smooth, thick bones of the skull completely encase the BRAIN in a chamber that has few natural points of entry. Vertebrae separated by cushions of cartilage enclose the SPINAL CORD, their irregular shapes deflecting access while at the same time permitting FLEXIBILITY. The ribs form a cage that contains the HEART and LUNGS, providing a framework for the bellows-like action of the lungs with the thick sternum like a shield to shelter the heart.

Form and function: the muscles The 650 or so muscles in the body give the body shape and make movement, including locomotion, possible. The skeletal muscles cover and protect the bones, attaching directly to them. Muscles also support and protect other structures such as BLOOD vessels and nerves. Most skeletal muscles work in opposing pairs, with one MUSCLE group contracting and the other relaxing in synchronization to permit the balanced, coordinated, and smooth move-

ments necessary for all body mobility from sitting to running.

Muscle cells form collective structures, muscle fibers, that are the functional units of movement. NERVE impulses from motor neurons (nerve cells that direct movement) travel from the NERVOUS SYSTEM to the muscle fibers. The NEUROTRANSMITTER acetylcholine facilitates the transfer of the impulse from the NEURON to the muscle fiber. Some muscle fibers remain in a state of partial contraction, providing muscle tone that supports posture. Other muscle fibers contract and relax in rapid sequence, providing muscle strength.

Connecting structures: tendons, ligaments, and fasciae Specialized structures of connective tissue join the bones and the muscles. Tendons, fibrous bands that arise from muscle, join muscle to bone. Ligaments are tough and sinewy; they connect bones to each other. Sheetlike FASCIA covers the muscles, connecting muscle to muscle and muscle to SKIN.

Articulating interfaces: the joints The ends of the bones come together in various ways that facilitate their movement. Hinge joints, such as the knee and the elbow, allow flexion and extension. Ball and socket joints, such as the hips and shoulders, allow rotational movement. The joints of the cranium—called sutures—are fused, allowing no movement at all. The vertebrae—the bones of the spine—have slight movement between each but collectively allow the body to bend in half.

Most joints contain cartilage, the body's most dense type of connective tissue, to cushion and protect the bones. Cartilage is very smooth, almost slick, permitting movement with minimal resistance. Synovial fluid lubricates larger joints, further reducing friction. A thin coat of cartilage covers the caps of the long bones in the arms and the legs. Thick pads of cartilage cushion the knees and the vertebrae, joints that bear considerable force with movement such as walking.

Biomechanics of movement Movement is a function of leverage and resistance that represents a complex and intricate interaction among the nerves, muscles, connective tissues, and bones. The cerebral cortex coordinates the numerous processes that make movement possible, integrating external sensory data with internal messages. A specialized sensory process, PROPRIOCEPTION, establishes unconscious awareness of the body's location within its physical environment. Proprioception helps the brain interpret and respond to the myriad messages about the body's relation to gravity and speed.

Harder than bone: the teeth The TEETH are the hardest structures in the body, formed of calcium and other minerals with a nearly impermeable enamel coating. The jaw bones—the maxilla (upper jaw) and the mandible (lower jaw)—anchor the teeth. Like most mammals, humans have two sets of teeth, the deciduous (sometimes called primary, milk, or baby teeth) and the permanent. Deciduous teeth begin to erupt through the gum line at about age four months; they drop out and permanent teeth replace them starting at about age six or seven years. The adult mouth contains 32 permanent teeth, generally occurring in pairs on each side of the mouth. They are of three major structures:

- Incisors and cuspids have sharp surfaces for cutting; these teeth are in the front of the mouth.
- Molars have flat surfaces for grinding and crushing; these teeth are in the back of the mouth.
- Bicuspids, sometimes called premolars, function somewhat as transitional structures, capable of secondary biting and preliminary chewing; they are in the middle of the jaw line.

Within the calcium cap is the tooth's living tissue, the pulp. Hollow extensions penetrate deep into the bones of the jaw, their protective canals encasing the nerves and blood vessels that supply the pulp. Chips and cracks in the enamel occur over time, weakening its protection and allowing BACTERIA to penetrate and begin to destroy the calcium cap, exposing the inner pulp. This kind of damage—dental caries (cavities)—is the leading oral health challenge. The teeth also facilitate speech, functioning like reflective walls to amplify sound and providing resistance for the tongue as it reshapes sound into words.

Health and Disorders of the Musculoskeletal System

The musculoskeletal system carries the human body hundreds of thousands of miles in the course of a typical lifetime. Trauma notwithstanding, it

does so with few "maintenance" requirements and little complaining. Proper nutrition and regular physical exercise are about all the bones, muscles, and connective structures require for most of life. However, the musculoskeletal system is vulnerable to numerous hereditary, congenital, and acquired health conditions. Trauma is the most significant risk to the musculoskeletal structures, particularly the limbs and joints. Sprains, strains, and fractures are common injuries. Over time, the repeated trauma of daily function also takes its toll. OSTEOARTHRITIS, the consequence of degenerative damage to the joints, is the most common musculoskeletal ailment, affecting as many as 60 million Americans.

Hereditary and congenital disorders can affect both the structure and function of the musculoskeletal system—and by extension, of other systems of the body as well. Connective tissue, the foundation of the musculoskeletal system, exists in nearly every body structure. Disorders of connective tissue such as MARFAN SYNDROME affect not only the skeleton and muscles but the walls of the arteries and the structure of organs. Though many movement disorders are neurologic in origin, disorders of muscle function such as MUSCULAR DYSTROPHY also affect mobility and motor function.

HEALTH CONDITIONS OF THE MUSCULOSKELETAL SYSTEM

ACHILLES TENDON INJURY
ACHONDROPLASIA
ADHESIVE CAPSULITIS
ANKLE INJURIES
ANKYLOSING SPONDYLITIS
ARTHROGRYPOSIS
BACK PAIN
BAKER'S CYST
BONE CANCER
BONE SPUR
BURSITIS
CARPAL TUNNEL SYNDROME
CERVICAL SPONDYLOSIS
CHARCOT-MARIE-TOOTH (CMT) DISEASE
CHONDRITIS
CONGENITAL HIP DYSPLASIA
CONTRACTURE
CRAMP
DISLOCATIONS
DYSTONIA
EPICONDYLITIS
FIBROMYALGIA
FRACTURE
GOUT
HERNIA
HERNIATED NUCLEUS PULPOSUS
INFECTIOUS ARTHRITIS
KNEE INJURIES
KYPHOSIS
LIPOMA
LORDOSIS
MARFAN SYNDROME
MUSCULAR DYSTROPHY
MYASTHENIA GRAVIS
MYOPATHY
MYOTONIA
NEUROGENIC ARTHROPATHY
OSGOOD-SCHLATTER DISEASE
OSTEOARTHRITIS
OSTEOGENESIS IMPERFECTA
OSTEOMALACIA
OSTEOMYELITIS
OSTEOPENIA
OSTEOPETROSIS
OSTEOPOROSIS
PAGET'S DISEASE OF THE BONE
PATELLOFEMORAL SYNDROME
PLANTAR FASCIITIS
POLYDACTYLY
POLYMYOSITIS
REITER'S SYNDROME
REPETITIVE MOTION INJURIES
RHABDOMYOMA
ROTATOR CUFF IMPINGEMENT SYNDROME
SCIATICA
SKELETAL DYSPLASIA
SPASM
SPINAL STENOSIS
SPRAINS AND STRAINS
SYNDACTYLY
SYNOVITIS
TALIPES EQUINOVARUS
TEMPOROMANDIBULAR DISORDERS
TENDONITIS
TORTICOLLIS

Traditions in Medical History

Not until the end of the Renaissance did physicians and scientists fully understand the structure of the human musculoskeletal system. The skeleton represented death; only without flesh was it visible. Seeing a bone, even in life, was never a good thing. Fractures, particularly compound fractures in which the bone ends broke through the surface of the skin, were frequently fatal. INFECTION was nearly inescapable. Fractures that did not kill often maimed; ancient doctors had little knowledge of biomechanics and without guidance from technology commonplace today, setting a fracture was at best an imprecise art.

The discovery of the X-RAY—electromagnetic energy capable of penetrating soft tissue—in the late 19th century finally gave doctors a means to examine the bones of living people. With X-ray doctors could see the bone ends of fractures and realign those ends for proper HEALING, and orthopedic medicine was born. Today X-ray remains the quintessential diagnostic tool for skeletal injuries.

Breakthrough Research and Treatment Advances

Today's technology allows incredible visualization of musculoskeletal structures, well beyond the black-and-white X-ray, and of musculoskeletal functions—with minimal intrusion into the body. Nucleotide bone scans, MAGNETIC RESONANCE IMAGING (MRI), ULTRASOUND, and COMPUTED TOMOGRAPHY (CT) SCAN allow doctors to "see" injuries such as torn ligaments, ruptured tendons, and stress fractures. Arthroscopy uses fiberoptic technology to

view the inside of a JOINT, providing a method of minimally invasive visualization for diagnostic and therapeutic purposes.

As in most areas of health and medicine, the most significant breakthroughs in research and treatment for musculoskeletal conditions comes from new discoveries in genetics. Researchers have identified many of the GENE mutations responsible for muscular dystrophy, for example. Though GENE THERAPY as treatment for genetically based musculoskeletal conditions remains experimental, the potential is great for treatments that can reverse the effects of gene mutations to halt and correct disease processes.

A

Achilles tendon A thick, strong band of connective tissue at the back of the heel that joins the gastrocnemius and soleus muscles of the calf (back of the lower leg) to the calcaneus (heel BONE). The Achilles TENDON makes possible extension of the foot, a necessary element of walking, running, and jumping. A sharp tap to the Achilles tendon with a REFLEX mallet causes the foot to jerk downward; this is the Achilles tendon reflex. Motor NEURON diseases such as AMYOTROPHIC LATERAL SCLEROSIS (ALS) and post-polio syndrome produce abnormal Achilles tendon reflex responses.

Injury to the Achilles tendon affects the ability to move the foot down. The Achilles tendon is vulnerable to damage during running and jumping, and especially "plant and twist" kinds of movements, common in numerous sports such as baseball, basketball, tennis, soccer, football, and running. The tendon may become inflamed (TENDONITIS) or tear (rupture).

For further discussion of the Achilles tendon within the context of musculoskeletal structure and function, please see the overview section "The Musculoskeletal System."

See also ACHILLES TENDON INJURY; LIGAMENT; POLIOMYELITIS.

Achilles tendon injury Traumatic damage to the ACHILLES TENDON, the broad band of connective tissue that joins the calf muscles to the heel of the foot. The most common Achilles TENDON injury is INFLAMMATION, called Achilles TENDONITIS, tends to develop somewhat gradually as an overuse injury. A tear in the Achilles tendon, called a rupture, generally happens suddenly during an athletic activity or event. Extended running, especially uphill or in shoes with flat heels (such as racing flats), and jumping are activities that place the Achilles tendon at risk for injury.

Achilles tendonitis causes PAIN and tenderness to touch at the base of the calf muscles on the back of the leg. The inflamed area may appear swollen. Though the pain may restrict the ability to use the foot and ankle, the mechanical functions of the Achilles tendon remain intact, and the person can perform the movements necessary to walk. Achilles tendonitis may follow a competitive event that places high stress on the legs, such as a race, or may develop during a new training regimen.

An Achilles rupture occurs suddenly during movement that stresses the Achilles tendon, such as running. The Achilles tendon is especially vulnerable to quick movements that place extreme stress on it, such as a "plant and twist" maneuver in sports such as tennis, soccer, basketball, soccer, and football. Runners may tear the Achilles tendon when starting from blocks or when accelerating for the finish. The injury causes a popping sensation, followed by pain and an inability to move the ankle and foot very well. When the tear is complete, severing the Achilles tendon, the person cannot point the foot downward to perform the basic movements of walking. Pain is most often at the back of the heel.

The ability to move the foot is generally the distinguishing factor between Achilles tendonitis and Achilles tendon rupture. The doctor's examination includes testing the Achilles tendon reflex, probing for areas of sensitivity (palpable divot), and watching the person move the feet with the legs dangling (seated on an examination table) and when walking. Diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and

ULTRASOUND can confirm the diagnosis though usually are not necessary unless the doctor suspects a complete rupture and needs to assess the extent and location of damage before surgery to repair it.

Most Achilles tendon injuries heal with ice, rest, and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to reduce inflammation and pain. The doctor may choose to cast the lower leg and foot to immobilize the ankle when the injury is severe. Surgery is usually necessary to repair significant or total Achilles tendon rupture. HEALING is complete when the person can move the injured foot with the same ease and range of motion as the uninjured foot, which may take six weeks to three months for repair and six months for rehabilitation, depending on the injury's severity. Swimming is an excellent activity for rehabilitation, as it allows full range of motion and use of the Achilles tendon without impact.

Stretching and WARM-UP before athletic activities, including WALKING FOR FITNESS, are the most effective methods for reducing the risk of injury to the Achilles tendon. People who have tight calf muscles or previous Achilles tendon injury benefit from regular stretching (once or twice daily) regardless of athletic activity.

See also ANKLE INJURIES; ATHLETIC INJURIES; BONE SPUR; SPRAINS AND STRAINS.

achondroplasia A genetic disorder in which the rate CARTILAGE cells (chondrocytes) convert to BONE cells is greatly slower than normal, resulting in skeletal abnormalities such as shortened limbs and diminished height. Achondroplasia is the most common cause of SKELETAL DYSPLASIA, commonly called dwarfism. Though achondroplasia can occur as an autosomal dominant inherited genetic disorder, it more commonly occurs as a spontaneous MUTATION of a GENE on CHROMOSOME 4 that encodes fibroblast growth factors, the proteins that regulate cartilage cell conversion. Prenatal testing can identify whether a FETUS has achondroplasia, though doctors generally offer the test only when there is reason to suspect the condition could be present or along with other GENETIC TESTING. Because infants born with achondroplasia have distinctive physical features, the disorder is obvious at birth.

The characteristics of achondroplasia include

- enlarged head and prominent forehead
- short arms and legs
- short hands and short, thick fingers with a distinct separation between the middle and ring fingers
- abnormalities in the opening at the base of the BRAIN, the foramen magnum, and in the vertebrae that compress the SPINAL CORD, affecting BREATHING
- craniofacial anomalies such as narrow nasal passages, flat NOSE, and short jaw

Evaluation for an infant born with achondroplasia typically includes COMPUTED TOMOGRAPHY (CT) SCAN, ULTRASOUND, or MAGNETIC RESONANCE IMAGING (MRI) to evaluate the extent of skeletal anomalies, especially those that may affect the spinal cord and thus vital functions such as breathing. Some infants also have or develop HYDROCEPHALY (fluid accumulation within the cranium), which may require a shunt for draining the excess fluid. As they grow, children who have achondroplasia are vulnerable to KYPHOSIS (a hump in the upper back) and LORDOSIS (curvature of the lower spine). They are also susceptible to frequent OTITIS media (middle EAR INFECTION) because the shortened facial structures mean the eustachian tubes, valvelike structures between the middle ear and the THROAT, are also shorter than normal and do not function properly.

Though some children may benefit from bone-lengthening operations, in most situations there are no treatments to normalize the development of bone. Bone-lengthening surgery is extensive and expensive, has significant risk for side effects (such as infection and permanent damage to the bones), and is controversial among medical experts. Some specialists use HUMAN GROWTH HORMONE (HGH) SUPPLEMENT early in the child's life, though this is also controversial and does not produce predictable results. Adults who have achondroplasia generally reach a maximum height of about four feet.

See also EUSTACHIAN TUBE; GENETIC COUNSELING; GENETIC DISORDERS; INHERITANCE PATTERN; OPERATION; SURGERY BENEFIT AND RISK ASSESSMENT.

adhesive capsulitis A condition in which the JOINT capsule of the shoulder joint fuses (adheres)

to the head of the humerus (long BONE of the upper arm), causing PAIN and constricting range of motion. Doctors do not know what causes adhesive capsulitis, commonly called frozen shoulder. The condition may be primary, in which there are no contributory conditions, or secondary, in which other conditions exist that may cause changes that allow adhesive capsulitis to develop. Adhesive capsulitis affects women somewhat more frequently than men and typically occurs in people over age 50.

Symptoms and Diagnostic Path

Adhesive capsulitis begins with acute pain in one shoulder that occurs for no obvious cause. Within weeks to months adhesions (scarlike tissue) develop that progressively limit the affected shoulder's range of motion. Most people first notice restricted movement when trying to reach up and behind, such as combing the HAIR, and when trying to reach back and behind, such as for a wallet in the pocket. The adhesions and range of motion restrictions progress until the person has very limited use of the shoulder. In most people the adhesions gradually lessen and the pain subsides over a period of one to three years. Doctors sometimes refer to the three stages of adhesive capsulitis as freezing, frozen, and thawing.

The pattern of symptoms is generally distinctive enough to allow diagnosis. The doctor may choose to perform diagnostic imaging procedures such as X-RAY or MAGNETIC RESONANCE IMAGING (MRI) to rule out other possible causes of the symptoms.

Treatment Options and Outlook

Because adhesive capsulitis is nearly always self-limiting, treatment primarily targets pain relief. Analgesic medications, heat, and PHYSICAL THERAPY in combination may improve range of motion. When symptoms are severe and do not respond to these measures, the doctor may recommend arthroscopic surgery to release the contractures. In most people such surgery relieves the pain and improves range of motion.

The entire course of adhesive capsulitis, treated nonsurgically, typically spans 1½ to 3 years, after which about half of people recover completely with no residual pain or restrictions on range of motion. In some people range of motion improves though remains limited. A few people experience residual pain and contractures that result in long-term disability.

Risk Factors and Preventive Measures

Conditions that appear to increase the risk for adhesive capsulitis include HYPERTHYROIDISM (overactive THYROID GLAND), DIABETES, and HYPERLIPIDEMIA (elevated CHOLESTEROL BLOOD LEVELS and TRIGLYCERIDE BLOOD LEVEL). Adhesive capsulitis is also more common in people who have SPINAL CORD INJURY, PARKINSON'S DISEASE, certain forms of NEUROPATHY, and traumatic injury to the structures of the shoulder. Despite these correlations, doctors do not know what initiates the onset of adhesive capsulitis and therefore do not know what measures may prevent its development.

See also CHRONIC PAIN; COMPLEX REGIONAL PAIN SYNDROME; SURGERY BENEFIT AND RISK ASSESSMENT.

aging, musculoskeletal changes that occur with

The muscles, connective tissues, and SKELETON arise from the mesoderm in the EMBRYO at about two weeks of gestational age. The skeleton's first form is as fibrous membranes (the bones of the cranium) or CARTILAGE. Through a process called ossification or osteogenesis, cartilage cells (chondrocytes) convert to BONE cells (osteoblasts, osteocytes, and osteoclasts). This early ossification uses the fibrous membrane (called intramembranous ossification) or the cartilage skeleton (called endochondral ossification) as a mold or template. Bone cells replace the connective tissue cells to form the bone matrix.

Areas of specialized bone tissue called secondary ossification centers form in the long bones; these become the epiphyses or growth plates. After birth the epiphysis extends through the growth of cartilage, which ossification then replaces as bone. The process extends through nearly the first two decades of life. Disorders of ossification include ACHONDROPLASIA, MARFAN SYNDROME, ACROMEGALY, and OSTEOGENESIS IMPERFECTA.

MUSCLE structures gain definition, mass, and STRENGTH as growth occurs. By four months of age a healthy infant can support his or her head and at about six months can sit unsupported and roll over from front to back or back to front. Between 8 and 12 months, an infant begins to crawl, throw

things, and pull into a standing position. By 14 months most infants are walking on their own, and by 18 months can run and jump. Motor skills—the ability to use the musculoskeletal system for mobility—continue to evolve throughout childhood. These skills, along with muscle mass and BONE DENSITY, peak in the late 20s.

By age 40, musculoskeletal structures and functions begin to decline. Joints begin to show the effects of wear. One health consequence of this is OSTEOARTHRITIS, which can become severe enough to warrant JOINT REPLACEMENT. Softening of the ligaments and other connective tissues makes joints more vulnerable to injury. Muscle mass and bone density gradually decrease, as does strength and FLEXIBILITY. In women these decreases become dramatic with MENOPAUSE, with the sudden and significant decline in estrogen. (Estrogen is one of the hormones that influences the movement of calcium between the BLOOD circulation and the bones.) The rate of decrease remains fairly constant in men, who have inherently larger amounts of muscle and bone.

However, by about age 75 or 80 gender differences balance out. Men and women alike have significantly less muscle tissue and bone structure, increasing susceptibility to injury from falls and other accidents. Though bone remodeling continues, it proceeds at a much slower pace. Other changes in the body may result in bone resorption outpacing bone rebuilding. The risk for neuromuscular disorders such as PARKINSON'S DISEASE also rises. At age 80, a woman may have lost four inches or more of her height as a consequence of musculoskeletal changes. Men also lose height, though typically not as dramatically.

See also ACCIDENTAL INJURIES; AGING, NEUROLOGIC CHANGES THAT OCCUR WITH; ESTROGENS; HIP FRACTURE IN OLDER ADULTS; HORMONE; LIGAMENT; RHEUMATOID ARTHRITIS.

amputation Removal or loss of a limb or body part. Amputation may be surgical, in which the removal is intentional to treat a disease condition, or traumatic, in which accidental injury results in the loss of the body part. Most amputations involve digits (fingers and toes) and limbs. In the United States, complications of DIABETES account for the majority of surgical amputations of the foot and lower leg; traumatic injury accounts for most upper extremity amputations. Other causes of amputation include uncontrollable OSTEOMYELITIS (INFECTION of the BONE), severe PERIPHERAL VASCULAR DISEASE (PVD), and tumors.

US surgeons perform nearly 200,000 amputations each year. Surgical amputation is a treatment of last resort, becoming an option only when other treatments fail and leaving the limb threatens the person's health. Surgical amputation is a major OPERATION performed in a hospital. For most amputations the person stays 2 to 10 days in the hospital.

Surgical Procedure

With the person asleep under general ANESTHESIA, the surgeon cuts through the SKIN and MUSCLE to reach the bone, structuring the incisions so tissue remains to create a flap that covers the surgical wound. The surgeon may need to use a saw to cut the bone, though in some circumstances the amputation takes place at the JOINT (called a disarticulation). For limb amputation the surgeon shapes the bone ends and remaining tissue to support a prosthesis.

When there is no infection or risk for infection is minimal, the surgeon closes the surgical wound by suturing the muscles together around the bone and pulling tissue and skin over the end in a flap.

Risks and Complications

The primary risks of amputation are excessive bleeding during surgery and infection and poor HEALING after surgery. The risk for infection is highest in people who have problems with BLOOD circulation in the extremities, such as may occur in PVD or diabetes. People who have diabetes may be slow to heal from the surgery of amputation, usually an extension of the complications of diabetes that made necessary the limb amputation. Complications such as failure to heal or spreading GANGRENE (dead tissue) require a follow-up surgery to attempt to improve the surgical wound for better healing.

Outlook and Lifestyle Modifications

Recovery and limitations depend on the type of amputation and the underlying health conditions. With focused PHYSICAL THERAPY and OCCUPATIONAL

THERAPY, most people can return to a satisfactory level of function and participation in many of the activities they previously enjoyed. A PROSTHETIC LIMB often allows nearly normal function. Adaptive devices and equipment can improve safety, mobility, and independence. People who have amputations as a result of severe chronic disease such as diabetes or PVD often find they have better QUALITY OF LIFE after amputation because the remaining tissue of the limb is healthy.

Amputation may be emotionally difficult for the person as well as for his or her loved ones. The loss of a body part may affect the person's self-image and self-esteem. Some people feel guilty about their health situations, and others feel angry or depressed. The health-care team generally includes a social worker or psychologist to help the person go through the grieving process and cope with the range of feelings and emotions.

See also ACCIDENTAL INJURIES; OCCUPATIONAL HEALTH AND SAFETY; PHANTOM PAIN; SURGERY BENEFIT AND RISK ASSESSMENT.

ankle injuries Sprains and fractures of the ankle resulting from accidental trauma. The ankle is vulnerable to twisting under the pressure of sudden, unexpected movement. Though ankle injuries are common ATHLETIC INJURIES, they also occur during routine activities such as stepping off a curb, walking on uneven surfaces, and walking in high heels. OBESITY AND HEALTH conditions that impair balance increase the risk for ankle injuries. Doctors in the United States treat about 4 million ankle injuries each year, most of which are sprains (injury to ligaments and tendons).

Three bones come together to form the ankle: the tibia and fibula, the long bones of the lower leg, and the talus, a platform-like BONE that forms the back of the foot. Three sets of strong ligaments hold these bones in place; equally strong muscles and tendons give the ankle range of motion. This structure is necessary because the ankle bears the body's weight. Transferring that weight from one foot to the other when walking places the equivalent of 1½ times the body's weight on the weight-bearing ankle and foot.

Most ankle injuries occur when the foot rolls inward, which stretches, tears, or otherwise damages structures on the outside of the ankle; these are lateral or inversion injuries. When the foot rolls outward, the damage occurs to the structures on the inside of the foot; these are medial or eversion injuries. A sharp blow or twist can break the base of the tibia or more commonly the fibula (the smaller of the lower leg bones). A severe LIGAMENT stretch or tear can pull a piece of the bone away, called an avulsion FRACTURE. Repeated stress such as occurs with intense running or jumping can cause stress fractures in the bones of the ankle or OSTEOARTHRITIS within the ankle JOINT.

Symptoms and Diagnostic Path

PAIN and swelling after a sudden twist or blow to the ankle are the typical symptoms of ankle injury. Both can be intense, and most people are reluctant to or cannot bear weight on the affected ankle. There is a strong correlation between the severity of symptoms, including the ability to walk or bear weight, and the type or seriousness of injury. When it is possible to bear weight on the ankle immediately following the injury and there is no pain to the lower portion of the fibula, fracture is unlikely. The doctor may order an X-ray of the ankle to rule out fracture.

Treatment Options and Outlook

The mainstay of treatment for ankle injuries of any kind is RICE—rest, ice, compression, and elevation. An elastic wrap may help support the injured ankle, though caution is necessary to make sure the wrap is not too tight, particularly during the first 48 hours when the ankle may continue to swell. The doctor may choose to cast a serious sprain. Fractures require casting or surgery or both. Casting is generally adequate for simple fracture in which the broken bone remains nondisplaced (stays in relative alignment). Displaced, comminuted, and open fractures typically require pins, screws, or plates to hold the bones in place while they heal. Sometimes this hardware remains in place and sometimes the surgeon removes it when HEALING is complete, depending on the nature of the fracture.

Most simple strains (injury to the muscles and tendons) heal in 4 to 6 weeks. A simple sprain (injury to the ligaments), which doctors may classify as grade 1 or grade 2, generally heals in 4 to 6 weeks. A severe sprain (grade 3) may take 12 to

16 weeks to fully heal. Doctors consider healing complete when the injured ankle can bear the body's weight without pain and with normal range of motion during normal activities, though very severe injuries may result in permanent limitations or laxity.

Risk Factors and Preventive Measures

Slipping, twisting, and falling are the most common risks for ankle injury. MOTOR VEHICLE ACCIDENTS, athletic activities that involve running and jumping, and recreational activities such as downhill skiing are also frequent causes of ankle injuries. People who are physically inactive or who have had multiple ankle strains may have WEAK ANKLES, a circumstance in which the ligaments supporting the ankle are soft or lax. Excessive body weight places further stress on the ankles and may cause the foot to turn inward, stretching the muscles and connective tissues in ways that limit their ability to provide stability during movement such as walking. OSTEOPOROSIS, a condition of diminished BONE DENSITY, makes the bones of the ankle vulnerable to fracture under circumstances that otherwise would not cause injury. Osteoporosis is a particular risk in women who are past MENOPAUSE and in men over age 65.

Regular weight-bearing activity such as walking helps strengthen the structures of the ankle. People who are prone to ankle injuries may choose to wrap, tape, brace, or otherwise support their ankles during activities that involve increased risk for unexpected twisting, such as running or sports. A physical therapist can teach specific exercises to strengthen weak ankles and improve FLEXIBILITY. WARM-UP exercises to stretch and loosen the ankles are important before engaging in physical activities. It is important to wear the right shoes for the activity, to give the foot and ankle proper support. Worn-out shoes, even if designed for the particular activity, increase the risk for injury.

See also ACHILLES TENDON INJURY; FLAT FEET; MUSCLE; PHYSICAL THERAPY; RESISTANCE EXERCISE; SHIN SPLINTS; SPRAINS AND STRAINS; TENDON; WALKING FOR FITNESS; WEEKEND WARRIOR.

ankylosing spondylitis A form of chronic, degenerative arthritis (INFLAMMATION of the joints) that primarily affects the spine. The inflammation permanently damages the vertebrae (bones of the spine), causing outgrowths of bony tissue that fuse vertebrae to one another such that their mobility and range of motion can become extremely limited. Ankylosing spondylitis, sometimes called Marie-Strümpell disease, is one of the AUTOIMMUNE DISORDERS related to RHEUMATOID ARTHRITIS. In most people who develop the condition, symptoms remain confined to the spine. However, in some people inflammation also involves structures of the EYE (IRITIS and UVEITIS), the HEART valves, the LUNGS, and other joints such as the shoulders and hips.

Symptoms and Diagnostic Path

Early symptoms of ankylosing spondylitis are general and include low BACK PAIN and stiffness, especially upon awakening. The PAIN often becomes intense at night, which is the primary reason any people seek medical evaluation. Over time the stiffness and pain may spread to the entire back, shoulders, and hips. As the condition progresses, additional symptoms may include loss of spine FLEXIBILITY and range of motion, constricted movement of the chest (from inflammation of the joints connecting the ribs to the spine), fatigue, and hunched or stooped posture.

The diagnostic path typically includes a comprehensive medical examination and PERSONAL HEALTH HISTORY, X-rays of the spine, and BLOOD tests to look for signs of inflammation within the body. Because symptoms are fairly general until the condition is well advanced, early diagnostic efforts look for more common causes such as OSTEOARTHRITIS.

Treatment Options and Outlook

Treatment typically combines prescription medications such as ANTI-INFLAMMATORY DRUGS (NSAIDS) and PHYSICAL THERAPY with lifestyle measures such as daily physical exercise, stretching and flexibility activities, and techniques to support upright posture. Some people experience symptom relief and delayed progression of the condition with medications used to treat rheumatoid arthritis, such as DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS). Though treatment cannot prevent the vertebrae from fusing, lifestyle measures can help retain

maximum functional capacity of the spine. Many doctors aim for a goal of shaping the fusion so the spine remains erect, which allows better mobility than when the spine fuses into a hunched posture. Ankylosing spondylitis is a lifelong condition.

Risk Factors and Preventive Measures

Ankylosing spondylitis typically begins before age 40 and is more common in men. It is also more common in people who have INFLAMMATORY BOWEL DISEASE (IBD) and in people of Native American heritage. Researchers have identified a GENE, HLA-B27, associated with ankylosing spondylitis. The HUMAN LEUKOCYTE ANTIGENS (HLAS) are proteins on the surfaces of cell membranes that identify the cells to the IMMUNE SYSTEM. HLA-B27 is one of the numerous genes that encodes for HLAs. Researchers believe this variant of the gene predisposes an individual for ankylosing spondylitis though does not inevitably result in the condition. Remaining as active as possible helps extend the spine's flexibility and range of motion.

See also CERVICAL SPONDYLOSIS; GENETIC PREDISPOSITION; REITER'S SYNDROME; ROUTINE MEDICAL EXAMINATION; X-RAY.

arthrogryposis The collective term for a group of congenital disorders, also called arthrogryposis multiplex congenita, in which multiple contractures restrict JOINT function throughout the body. Joints may be partially or completely fused. Researchers believe about 30 percent of arthrogryposis develops when the FETUS is not able to move freely in the UTERUS before birth. The restricted movement causes muscles and connective tissues such as tendons and ligaments to grow abnormally around the immobile joints, fixing them in their positions. Circumstances that may restrict fetal movement include

- insufficient AMNIOTIC FLUID
- abnormalities of the uterus
- large UTERINE FIBROIDS
- twins or other multiples
- neurologic and other developmental anomalies in the fetus, such as MUSCULAR DYSTROPHY or MITOCHONDRIAL DISORDERS, that inhibit normal movement

Symptoms and Diagnostic Path

The doctor may suspect arthrogryposis when the pregnant mother reports that the movements of her unborn baby are infrequent. ULTRASOUND can detect the changes in soft tissue structure and BONE fusions at the joints before birth; the joint deformities are obvious at birth. The delivery of an infant who has arthrogryposis may be challenging when the affected joints prevent normal passage through the birth canal. The obstetrician may recommend CESAREAN SECTION to avoid injury to infant and mother. Ultrasound after birth may provide additional information about the extent to which contractures affect the infant's joints as well as help doctors determine whether there are other anomalies present.

Treatment Options and Outlook

Treatment depends on the extent of the contractures though typically combines surgery to correct joint deformities and casting with aggressive PHYSICAL THERAPY to restore as much function as possible. Surgery can relieve the abnormal tension shortened connective tissue and MUSCLE structures place on the joints, and the surgeon often can reconstruct more functional alignments to improve movement of the joint. Surgery may also restructure bone tissue, generally in multiple operations timed with growth patterns throughout childhood. Physical therapy helps strengthen the tissues and extend range of motion.

Although the deformities are permanent, they are not progressive; thus the condition does not worsen as the child grows. Aggressive treatment early in life may allow a relatively normal lifestyle in late childhood and adulthood when contractures are mild to moderate. Severe contractures tend to result in permanent disabilities that require adaptive techniques and devices for mobility.

Risk Factors and Preventive Measures

Inability of the fetus to move freely in the uterus is the primary risk factor for arthrogryposis. Pregnancies in women who have neuromuscular disorders such as MYASTHENIA GRAVIS, MULTIPLE SCLEROSIS, or MYOTONIA are at higher risk. Extended high FEVER during PREGNANCY, such as may occur with serious INFECTION, may affect the development of the fetus in ways that impair muscle, connective

tissue, and NERVE structure and function. These impairments secondarily affect joint function.

About 30 percent of arthrogryposis is hereditary, though affected parents may have such mild symptoms that they do not know they have the condition. When one or both parents have arthrogryposis, there is increased risk the infant will also have the condition. GENETIC TESTING and GENETIC COUNSELING may help such parents evaluate their risk and make FAMILY PLANNING decisions.

See also CONGENITAL ANOMALY; CONTRACTURE; GENETIC DISORDERS; LIGAMENT; SURGERY BENEFIT AND RISK ASSESSMENT; TALIPES EQUINOVARUS; TENDON.

arthroscopy A MINIMALLY INVASIVE SURGERY procedure that allows an orthopedic surgeon to view the inside of a JOINT using a lighted, flexible endoscope adapted for this use, called an arthroscope. Arthroscopy, also called arthroscopic surgery, has both diagnostic and therapeutic applications. Inserted into the joint through a small incision, the arthroscope has a tiny camera at its tip that sends images to a monitor. The orthopedic surgeon manipulates the arthroscope and specially designed instruments to examine the joint and repair damage to CARTILAGE, LIGAMENT, TENDON, and other tissues. Arthroscopy has largely replaced OPEN SURGERY for most operations on the joints except JOINT REPLACEMENT.

Surgical Procedure

The orthopedic surgeon performs arthroscopy in a hospital operating suite or an AMBULATORY SURGERY facility. Most arthroscopies are same-day (outpatient) procedures, with the person arriving a few hours before the scheduled arthroscopy and going home a few hours after the surgeon completes the procedure. ANESTHESIA may be regional (a NERVE block that numbs the limb) or general (puts the person to sleep). The orthopedic surgeon makes two or more small incisions around the JOINT: one for the insertion of the arthroscope, one for insertion of the irrigating catheter, and others for insertion of the arthroscopic instruments. Most arthroscopic procedures take 20 to 60 minutes.

After the arthroscopic operation, the person rests in the recovery area until the anesthetic is fully worn off and the person is comfortable enough to go home. Generally the person receives mild to moderate ANALGESIC MEDICATIONS for PAIN relief, depending on the extent of discomfort he or she feels. Because the entry into the joint is minimal, many people experience little discomfort or pain after the procedure.

Risks and Complications

As with any surgical procedure, arthroscopy has a risk for excessive bleeding and INFECTION. However, these complications are uncommon. Soreness and bruising at the incision sites is common though usually mild. When the arthroscopic examination reveals more extensive damage than the orthopedic surgeon can repair arthroscopically, the operation may become an open surgery with longer recovery and rehabilitation periods.

Outlook and Lifestyle Modifications

Most people recover from arthroscopic procedures fully and without complications, returning to their regular activities within several days to two weeks, depending on the surgeon's recommendation and the type of procedure. Arthroscopic procedures generally repair injuries that have limited the person's mobility or function, so most people are much improved after their operations and may return to activities their injuries had prevented them from performing.

See also ENDOSCOPY; MENISCECTOMY; SURGERY BENEFIT AND RISK ASSESSMENT.

athletic injuries ACCIDENTAL INJURIES that occur during athletic activities or sporting events. Though a certain degree of risk is inherent in athletic events, particularly competitions, most athletic injuries occur for three main reasons. They are

- inadequate CONDITIONING or TRAINING
- insufficient WARM-UP and pre-event preparation
- inappropriate or improperly fitted clothing, shoes, equipment, or protective gear

Athletic injuries may be acute (occur suddenly) or chronic (develop over time). The most common acute injuries are SPRAINS AND STRAINS—damage to the soft tissue structures of the musculoskeletal system. Also common are fractures and open wounds (cuts and scrapes). Chronic injuries among recreational, collegiate, and professional athletes gener-

ally arise from overuse and may result in discomfort and limitations of use long after athletic participation ends. OSTEOARTHRITIS, EPICONDYLITIS, and PATELLOFEMORAL SYNDROME are the most common chronic injuries among athletes.

Training and conditioning activities that improve overall STRENGTH, FLEXIBILITY, and ENDURANCE can significantly reduce the risk for injury. Equally important is proper technique (including clothing and equipment) for the activity. It is worthwhile to attend clinics and classes for specific activities to learn methods and techniques that both improve performance and reduce the risk for injury. Most athletic injuries are preventable.

COMMON ATHLETIC INJURIES

ACHILLES TENDON INJURY	ANKLE INJURIES
BLISTER	BURSITIS
CHAFING	CHARLEYHORSE
CONCUSSION	contusion (bruising)
CRAMP	DISLOCATIONS
EPICONDYLITIS	fasciitis
FRACTURE	KNEE INJURIES
LACERATIONS (cuts and scrapes)	PATELLOFEMORAL SYNDROME
SHIN SPLINTS	SPRAINS AND STRAINS
STINGER	TENDONITIS

See also BLISTER PREVENTION; CROSS-TRAINING; DISABILITY AND EXERCISE; YOGA.

B

back pain PAIN that arises from injury to the structures of the spine. Most back pain involves the soft tissue structures—muscles, ligaments, tendons, and CARTILAGE. Back pain is very common, affecting nearly every adult at some time in his or her lifetime and is second only to HEADACHE as a reason for missing work. Though most back pain heals without residual consequences, chronic back pain (back pain that continues beyond three to six months) remains the leading cause of occupational disability.

Acute back pain develops suddenly, a consequence of traumatic injury or surgery, and improves when the underlying cause improves. The low back (lumbar spine) and the neck (cervical spine) are the most vulnerable to traumatic injury. Low back strain is a common injury often related to overuse, incorrect lifting (including lifting too much weight), and sudden twisting movements. Cervical strain often results from incorrect posture, especially prolonged sitting in the same position, or whiplash-type trauma in which the head moves suddenly and more rapidly than the body in a whipping fashion that stretches muscles and ligaments. Chronic back pain is pain that exists or continues when there is no pathologic reason and more often affects the low back.

Back PAIN with accompanying numbness or weakness in the legs may indicate damage to NERVE structures. Neck pain with FEVER or headache may indicate serious INFECTION (ENCEPHALITIS or MENINGITIS). These circumstances require immediate medical evaluation.

Symptoms and Diagnostic Path

Back pain, whether acute or chronic, may be sharp, dull, shooting, persistent, intermittent, or achy in character. The nature and location of the pain sometimes helps the doctor determine the cause. Most back pain results from soft tissue injury; unless there are neurologic symptoms, such as weakness or numbness in the legs or arms, the doctor may recommend a trial of conservative treatment before progressing to diagnostic testing. Pain that persists requires further diagnostic effort that may include X-RAY, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI). These imaging procedures help the doctor visualize the structure of the spine to determine whether there is deterioration or other injury that could be pressing on spinal NERVE roots and other structures of the back to produce pain.

Treatment Options and Outlook

Most acute back pain improves with conservative treatment to relieve INFLAMMATION. Such treatment may include alternating heat and cold to the area of pain, ANALGESIC MEDICATIONS for pain relief, NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve inflammation and pain, and sometimes MUSCLE RELAXANT MEDICATIONS when MUSCLE spasms are a problem. Some doctors recommend a day or two of relative inactivity to allow the back muscles to rest and relax, though some studies show HEALING occurs more rapidly in mild to moderate back pain when people continue their regular activities (except strenuous exercise or heavy lifting).

Treatment for chronic back pain depends on what underlying reasons the doctor can identify that could be accountable. Complementary methods such as ACUPUNCTURE, various types of MASSAGE THERAPY, CHIROPRACTIC manipulation, and OSTEO-

PATHIC MANIPULATIVE TREATMENT (OMT) often provide relief. YOGA and PHYSICAL THERAPY are methods for improving FLEXIBILITY and STRENGTH after the initial injury heals.

Risk Factors and Preventive Measures

Key risk factors for back pain include occupational risk (jobs that require heavy lifting, pushing, or pulling), OBESITY, physical inactivity, and cigarette smoking. Most back pain occurs as a result of injury to the back, commonly strained muscles or sprained ligaments. Regular physical exercise to maintain strength and flexibility reduces the risk for such injury and aids in weight loss efforts when excessive body weight is a factor. Proper lifting technique and good posture are also important.

See also ACUTE PAIN; ANKYLOSING SPONDYLITIS; CERVICAL SPONDYLOSIS; CHRONIC PAIN; CONDITIONING LIGAMENT; OSTEOARTHRITIS; SCIATICA; SPASM; SPINAL CORD INJURY; TENDON.

Baker's cyst A fluid-filled sac, also called a popliteal cyst, that forms at the back of the knee. The cyst develops when there is a tear in the synovial capsule (the membranous structure containing the fluid that lubricates the JOINT) that allows synovial fluid to leak into the ears of least resistance, which is the popliteal fossa. The leaking fluid bulges out from the knee joint or forms a connection with a BURSA in the back of the knee. Either circumstance allows synovial fluid to collect, forming a noticeable lump behind the knee. A Baker's cyst is soft to the touch and usually painless, though a large cyst can be uncomfortable or painful with movement or pressure.

NOTHING TO DO WITH BAKING

It is a common assumption that the term Baker's cyst has something to do with being a baker, just as bricklayer's shoulder tends to afflict bricklayers and tennis elbow develops in people who frequently play tennis (both conditions are forms of BURSITIS). But Baker's cyst takes its name from the British surgeon who first identified it: William Morrant Baker (1839–1896).

When the cyst causes PAIN, the doctor may use MAGNETIC RESONANCE IMAGING (MRI) to determine whether other factors are involved. Occasionally a Baker's cyst is a symptom of a torn meniscus (CARTILAGE in the knee), in which case treatment such as surgery may be necessary. Nearly always a Baker's cyst eventually goes away without treatment.

See also ARTHROSCOPY; BURSITIS; KNEE INJURIES; OSTEOARTHRITIS; SYNOVITIS; TENDONITIS.

bone The rigid tissue that gives the body structure and mobility. Bone consists of living cells contained within a mineralized structure called the bone matrix. Collagen fibers form intricate networks to which crystals of calcium phosphate, calcium carbonate, and other mineral compounds adhere, forming the dense and rigid structure familiar as bone. Despite its density and its impression as a static structure, bone is in a perpetual state of change, called remodeling. Throughout life certain processes destroy old bone and other processes construct new bone.

Bone Cells

Three types of cells make up bone tissue:

- Osteoblasts form new bone. In response to stimulation from hormones such as CALCITONIN, ESTROGENS, and TESTOSTERONE, osteoblasts draw calcium and other minerals into the bone to strengthen and solidify the bone matrix. Osteoblasts produce a collagen-based substance called osteoid. Calcium, phosphorus, magnesium, and other minerals bind with the osteoid to form mineralized bone (the bone matrix).
- Osteocytes make up the structure of existing bone. Contained within the bone matrix, osteocytes have a lifespan of 20 years or more. Osteocytes begin their lives as osteoblasts, then become enclosed in the bone's mineralized structure. The spaces they occupy within the mineralized framework are lacunae. Each lacuna has a rich BLOOD supply to nourish and support the osteocytes.
- Osteoclasts remove old bone. Osteoclasts derive from monocytes and are phagocytic; they encircle and consume cellular debris. As they consume old bone tissue, osteoclasts release its calcium into the blood circulation. PARATHYROID

HORMONE plays a key role in regulating this release. The process of bone resorption leaves vacant lacunae on the surface of the bone that subsequently fill with new bone structure.

In health, osteoblasts and osteoclasts function in relative balance so the rate of new bone formation matches the rate of old bone destruction. This process of bone remodeling is one of maintenance, not growth. Bone growth, in which the bones increase in size, occurs through ossification (conversion of CARTILAGE cells to bone cells). Imbalance may result from disease processes that alter HORMONE levels in the body or when calcium levels in the blood circulation are too low. Calcium is vital to numerous cellular activities and crucial for MUSCLE contraction and the conduction of NERVE signals; when its levels in the blood circulation are inadequate, the body accelerates bone resorption so it can withdraw calcium from the bones.

Bone Structure

Were they solid, bones would weigh more than the body could support or the muscles could move. So instead they are a combination of densities that provide a balance between STRENGTH and mass. Though all bones contain the same elements of structure, the particular combination of those elements varies according to the bone's role.

The outermost layer of bone, called compact bone or cortical bone, is made of multiple thin layers, called lamellae, that contain tightly packed osteocytes. Each lamella contains a somewhat different structure of cells, altering the density and orientation of the bone structure for maximum strength. Compact bone is heavily mineralized and very dense; tooth enamel is the only other substance in the body that is harder than compact bone. An intricate network of canals, called the Haversian systems, bring blood vessels and nerves through the lamellae to nourish and support communication among the osteocytes. Compact bone protects the inner bone structures and provides the stiffness necessary to leverage the muscles for movement.

The middle layer of bone is cancellous, or spongy, bone, also called trabecular bone, where mineralized filaments form intricate networks of walls and spaces. The spaces contain osteocytes, fluids, and other cells. The structure of cancellous bone is more elastic than that of compact bone, allowing the bones to absorb compression such as occurs with walking, running, and jumping. Cancellous bone has less than half the density of compact bone but many times more the surface area.

Some bones contain a center channel, the medullary canal, that houses BONE MARROW. In children every bone contains red bone marrow, the type of bone marrow that produces new blood cells. By adulthood only the long bones, sternum, and hip bones contain appreciable amounts of red bone marrow. Yellow bone marrow, a mix of collagen and fatty tissues, occupies the innermost layer of most other bones. Some bones do not contain any marrow.

A thin but tough membrane called the periosteum covers the surface of the bones except at the joints. It forms the attachment surface for tendons and ligaments. The periosteum contains a rich network of blood vessels and nerves that help nourish the compact bone. Osteoblasts in the periosteum are "first responders" when there is injury to the bone, rapidly forming new bone for repair. The nerves in the periosteum are largely responsible for PAIN signals when there is injury to the bone.

Types of Bones

The SKELETON contains four basic types of bones: long, short, flat, and irregular. Long bones, such as those in the arms and legs, must support the body's weight and mass. Their length and structure also allows them to function as levers to make movement possible. A thin layer of compact bone provides the rigidity the long bones require; a substantial middle layer of cancellous bone provides added bone mass for strength and stability. The intricate trabecular structure of cancellous bone makes it much stronger for supporting weight, though more vulnerable to impact. At each end of a long bone is the epiphysis, or growth plate, where ossification takes place during growth in childhood. The shaft of a long bone is its diaphysis. Lengthwise through the center of a long bone is a medullary canal that contains bone marrow.

Short bones, such as those that form phalanges (metacarpals in the fingers and metatarsals in the toes), are structurally long bones on a much

smaller scale. However, a short bone does not have a medullary canal or bone marrow. Flat bones, such as the scapulae (shoulder blades), sternum (breastbone), and pelvis (hip bones), serve as attachment surfaces for the large muscles of movement. They contain a substantial thickness of compact bone with a thin layer of cancellous bone in the center. The sternum and the pelvis also contain bone marrow. Irregular bones, such as the vertebrae (bones of the spine), carpals (bones of the wrist), and tarsals (bones of the ankle), are primarily structures of compact bone with cancellous bone centers.

Bone Health and Disease

Bones require a steady intake of dietary calcium and other minerals as well as an adequate amount of vitamin D, VITAMIN K, and various hormones to maintain themselves. Deficiencies (and less commonly, excesses) of these substances alter bone structure in ways that can affect bone function. Though a certain degree of demineralization occurs naturally as a component of the aging process, excessive calcium loss results in thin and weak bones that are particularly vulnerable to FRACTURE. Fracture is the most common health condition that affects the bones. Other health conditions involving the bones include OSTEOPOROSIS, INFECTION (OSTEOMYELITIS), and congenital musculoskeletal anomalies (BIRTH DEFECTS that affect muscle and bone structure and function).

HEALTH CONDITIONS THAT AFFECT THE BONES

ACHONDROPLASIA	arthrogryposis
BONE cancer	BONE SPUR
cleft palate	FRACTURE
KYPHOSIS	LORDOSIS
MARFAN SYNDROME	OSGOOD-SCHLATTER DISEASE
OSTEOGENESIS IMPERFECTA	OSTEOMALACIA
OSTEOMYELITIS	OSTEOPENIA
OSTEOPOROSIS	POLYDACTYLY
RHEUMATOID ARTHRITIS	SCOLIOSIS
SKELETAL DYSPLASIA	SPINA BIFIDA

For further discussion of bone structure and function, please see the overview section "The Musculoskeletal System."

See also AGING, MUSCULOSKELETAL CHANGES THAT OCCUR WITH; CALCIUM AND BONE HEALTH; CLEFT PALATE/CLEFT PALATE AND LIP; JOINT; LIGAMENT; MONOCYTE; MUSCLE; PHAGOCYTE; SKELETON; TENDON.

bone cancer Cancer that occurs in the tissues of the BONE, either as primary cancer (cancer that originates in the bone) or metastatic cancer (cancer that spreads to the bone from an origin elsewhere in the body). Primary bone cancer is rare; doctors in the United States diagnose about 2,500 people with primary bone cancer each year. Its three forms are

- osteosarcoma, which arises from osteoid (the formative tissue of new bone) usually in the upper leg or upper arm in young people ages 10 to 25
- Ewing's SARCOMA, which results from a TRANSLOCATION GENE MUTATION and generally arises from the long bones (and occasionally soft tissue structures) during ADOLESCENCE
- chondrosarcoma, which develops in the cartilage of the shoulders or pelvis in adults over age 50

Osteosarcoma accounts for about a third of primary bone cancers. RADIATION THERAPY for other cancers increases the risk for osteosarcoma. Though primarily a cancer of childhood, osteosarcoma sometimes occurs in older adults. Oncologists (cancer specialists) often stage primary bone cancer only as localized (one contained site) or metastasized (spread to multiple sites).

The bone is a common site for cancer that metastasizes from other sites in the body such as the BREAST, PROSTATE GLAND, and COLON. Metastatic cancer retains the name of its original site. Multiple myeloma, a cancer of the BLOOD, also affects bone structure though is not a true bone cancer.

Symptoms and Diagnostic Path

The main symptom of bone cancer is PAIN, usually at the site of the tumor. The pain may be present for several months before becoming intense enough for the person to seek treatment, or may develop suddenly. Sometimes the first indication of bone cancer is a FRACTURE, either spontaneous (without trauma) or as a consequence of minor trauma that would not fracture healthy bone. The diagnostic path typically begins with X-rays, which can show

most bone cancers. COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), and radioisotope bone scan can provide greater detail about the tumor to aid in its diagnosis. POSITRON EMISSION TOMOGRAPHY (PET) SCAN can detect whether or to what extent the cancer has metastasized to other sites in the body. A blood test to measure the level of alkaline phosphatase, an enzyme osteoblasts release when configuring new bone tissue, may suggest—though cannot confirm—bone cancer. Blood levels of this enzyme are normally high during periods of bone growth. Biopsy of the tumor provides the definitive diagnosis.

Treatment Options and Outlook

Treatment depends on the location and size of the tumor. Treatment options for primary bone cancers include CHEMOTHERAPY, radiation therapy, and surgery to remove the tumor. Often, radiation therapy or chemotherapy administered first can shrink the tumor so the surgeon can remove it without the need to amputate the involved limb. Oncologists often administer chemotherapy both before and after surgery. The course of chemotherapy before surgery is typically 8 to 10 weeks; chemotherapy after surgery may extend for a year. The oncologist is likely to add radiation therapy to the treatment regimen when there are metastases the surgeon cannot safely remove. Treatment for metastatic cancer of the bone depends on the type of primary cancer and the degree of METASTASIS.

The outlook after treatment depends on the extent of cancer present at the time of diagnosis. Significant surgery, such as AMPUTATION, requires intensive rehabilitation. The outlook for metastatic cancer of the bone depends on the type of primary cancer and the aggressiveness of metastatic disease.

Risk Factors and Preventive Measures

Though Ewing's sarcoma has a clear genetic connection, doctors know little about the risk factors for and causes of other forms of primary bone cancer. Radiation exposure, such as radiation therapy to treat a different cancer, increases the risk for osteosarcoma. There are no measures known to prevent bone cancer.

See also BREAST CANCER; CANCER TREATMENT OPTIONS AND DECISIONS; COLORECTAL CANCER; PAGET'S DISEASE OF THE BONE; PROSTATE CANCER; SURGERY FOR CANCER.

bone density The amount of mineral, primarily calcium, the bones contain that gives them their mass. BONE density is important to give the SKELETON enough structure to support the body. Insufficient bone density results in the bone loss conditions OSTEOPENIA and OSTEOPOROSIS. Numerous hormones participate in maintaining bone density. Among them are estrogen, TESTOSTERONE, CALCITONIN, vitamin D (in the form of calciferol), and PARATHYROID HORMONE. Though calcium is the mineral most commonly associated with bone structure and bone density, other minerals that also are important, including magnesium and phosphorus.

Bone density naturally diminishes with increasing age, beginning at about age 35, at a rate of about 2 percent per year. Because estrogen is particularly essential for maintaining bone density in women, bone density drops precipitously at MENOPAUSE when a woman's estrogen production drops to nearly nothing. Because men's bodies are larger, they inherently have greater bone mass. Testosterone contributes to this mass, as it does a man's greater MUSCLE mass. The natural decrease in bone density is usually not a health concern until a man reaches his middle to late 60s.

Disorders of Bone Density

Most health problems related to bone density arise from diminished bone mass, which presents increased risk for bone FRACTURE. Spontaneous fracture (fracture that occurs without trauma or other cause) is possible when bone density is very low. The spine and the hip are at particular risk. The most common of these conditions are osteopenia (bone loss that places the individual at increased risk for fracture) and osteoporosis (bone loss that places the individual at significant risk for fracture). Compression fractures of the spine, in which the vertebrae collapse, can endanger the SPINAL CORD; HIP FRACTURE IN OLDER ADULTS is a key cause of disability and death. Medications are available that stimulate bone growth, helping restore lost bone mass. The doctor may prescribe such medications, along with lifestyle measures such as RESISTANCE EXERCISE, to increase bone density. Excessive bone mass is far less common

though may occur in conditions such as OSTEOPETROSIS.

Bone Density Testing

A number of tests can measure bone density. Among them are

- dual energy X-RAY absorptiometry (DEXA or DXA), which uses low-DOSE X-ray to measure the bone mass in the spine and hip
- peripheral dual energy X-ray absorptiometry (pDEXA or pDXA), which uses low-dose X-ray to measure the bone mass in the wrist or heel
- single-energy X-ray absorptiometry (SXA), which uses low-dose X-ray to measure the bone mass in the wrist or heel
- quantitative ULTRASOUND, which uses sound waves to measure the bone mass in the heel, patella (kneecap), and tibia (long bone in the lower leg)
- quantitative computed tomography (QCT), which uses X-ray to measure the bone mass in the spine
- peripheral quantitative computed tomography (pQCT), which uses X-ray to measure the bone mass in the wrist

DEXA provides the most detailed information and is simple to perform. QCT and pQCT are variations of COMPUTED TOMOGRAPHY (CT) SCAN that use somewhat higher doses of X-ray and are more complex to perform but can be more reliable in people who have already had fractures of the spine or hip. Mobile clinics and even some pharmacies use peripheral methods for screening. All testing methods to measure bone density are painless, noninvasive, and take 20 minutes or less to complete.

Bone density tests report two scores:

- The T-score compares an individual's bone density to a figure that represents the bone density of a healthy adult in his or her mid-20s, the period when bone density is at its highest. The comparison is gender specific.
- The Z-score compares an individual's bone density to a figure that represents other adults of the same age. The Z-score comparison is also gender specific.

Because older adults have lower bone mass, the Z-score is less significant than the T-score for assessing the presence of osteopenia and osteoporosis. Generally the T-score and the Z-score correlate; a person who has a low T-score also has a low Z-score.

The difference between an individual's bone density score and the representative standard score is the standard deviation (SD), reported as a positive (+) or negative (–) figure. Each full SD represents about 10 percent of normal bone mass. The lower the T-score, the greater the percentage of bone loss. A T-score that is 2.5 SDs or more below the norm (–2.5) is the diagnostic marker for osteoporosis.

BONE DENSITY SCORES

Diagnostic Category	T-Score	Z-Score
healthy	–1 or higher	–1 or higher
OSTEOPENIA (increased risk for fracture)	–1 to –2.5	–1 to –2.5
OSTEOPOROSIS (significant risk for fracture)	below –2.5	below –2.5

See also ESTROGENS; HORMONE; OSTEOMALACIA.

bone spur An extension of BONE tissue, also called an osteophyte, that commonly develops near a JOINT. A bone spur has a jagged, pointed appearance. Doctors believe bone spurs develop as a means of protecting a joint exposed to excessive stress or disease process. Most bone spurs do not cause symptoms, though may be apparent as bumps in the MUSCLE or other soft tissue. Bone spurs cause PAIN when they irritate surrounding tissues such as MUSCLE and CARTILAGE. Bone spurs are especially common in the heels, hands, shoulders, and spine.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) often succeed in relieving the INFLAMMATION and pain. For bone spurs that cause substantial pain, the doctor may inject the site with cortisone and a topical anesthetic agent to reduce inflammation and relieve pain.

See also ACHILLES TENDON INJURY; REPETITIVE MOTION INJURIES.

bursa A fluid-filled sac between layers of MUSCLE that buffers the movement of muscles against each

other. A synovial membrane, which secretes a lubricating fluid (synovial fluid), lines the inside of the bursa. This is the same kind of membrane and fluid that encloses and lubricates the joints. Most people have between 130 and 160 bursae throughout their bodies, typically located near joints. Bursae are vulnerable to INFLAMMATION (BURSITIS) and fibrosis (scarring), both of which cause pain and interfere with the bursa's proper function.

For further discussion of bursae within the context of musculoskeletal structure and function, please see the overview section "The Musculoskeletal System."

See also CARTILAGE; JOINT; LIGAMENT; TENDON.

bursitis INFLAMMATION of a BURSA, a fluid-filled sac between muscles or between muscles and BONE that protects tissues from friction during movement. Bursitis is a common condition often associated with overuse of particular joints though the joints themselves are normal. Casual terminology for bursitis often relates it to the activities that precipitate it, such as tennis elbow. Accidental falls and blunt blows over bursae may also cause bursitis, particularly of the deep bursae. Bursae near the shoulder, elbow, hip, and knee are most often affected. An adult has 130 to 160 bursae throughout the body, any of which may become inflamed.

The primary symptoms of bursitis are PAIN and swelling in the area of the involved bursa. When there is also FEVER, an INFECTION may be the cause of the bursitis. Bursitis due to infection often requires surgical debridement (opening the bursa to remove damaged tissue and accumulated pus) and treatment with ANTIBIOTIC MEDICATIONS. Intermittent cold packs over the affected area during the first 48 hours of symptoms may slow inflammation and relieve pain. After 48 hours intermittent heat provides greater relief. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) further relieve inflammation and pain.

Most bursitis improves in two to six weeks with such treatment. The doctor may inject a steroid medication, alone or in combination with a local anesthetic agent, into a bursa that is causing severe or chronic pain and restricting range of motion. Though resting the affected JOINT is helpful in the early stages when the bursitis is most uncomfortable, regular physical activity hastens HEALING and maintains full function of the joint.

See also MUSCLE; OSGOOD-SCHLATTER DISEASE; OSTEOARTHRITIS; REPETITIVE MOTION INJURIES; RHEUMATOID ARTHRITIS; TENDONITIS.

C

calcium and bone health The correlation between dietary intake of calcium and the density and STRENGTH of the bones. Calcium is essential for proper BONE structure, strength, and mass. The bones contain about 99 percent of the calcium in the body. From before birth until about age 30, the body adds calcium and other minerals to bone tissue to increase bone mass and strengthen the skeletal structure. The SKELETON reaches peak bone mass and strength in the late 20s. After age 30, bone mass begins to decrease. With increasing age after 30 the body's ability to absorb dietary calcium diminishes. Cigarette smoking and long-term excessive ALCOHOL consumption accelerate the decrease. It is important for long-term bone health that peak bone mass be as high as possible. Regular weight-bearing exercise, such as walking and running, stimulates the growth of new bone tissue.

BONES: THE BODY'S CALCIUM BANK

Calcium is a vital mineral for many activities in cells throughout the body, including the conduction of NERVE signals and the contraction of MUSCLE cells. The body uses the calcium stores in the bones to meet its other needs for calcium when dietary intake does not meet those needs and calcium in the BLOOD circulation drops. CALCITONIN and PARATHYROID HORMONE are the hormones that primarily regulate calcium transport between the blood circulation and the bones.

Without adequate calcium the bones can become dangerously thin and weak, making them susceptible to FRACTURE under circumstances that otherwise would not harm the bones. The key health conditions of inadequate BONE DENSITY are OSTEOPENIA and OSTEOPOROSIS. Osteoporosis is the leading cause of HIP FRACTURE IN OLDER ADULTS, which often results in long-term disability or premature death. Though loss of bone density with aging is inevitable, lifelong measures such as adequate calcium intake and daily weight-bearing exercise can maintain bone health and prevent osteoporosis.

The body must obtain calcium through dietary sources or supplements. The amount of calcium an individual needs changes across the spectrum of age. The years of ADOLESCENCE are among the most vulnerable for inadequate calcium consumption because teens tend to drink much less milk and eat fewer dark green vegetables, the primary dietary sources of calcium in the American diet.

CALCIUM INTAKE NEEDS

Age	Daily Adequate Intake (AI) Amount of Calcium
birth to 3 years	500 milligrams (mg)
4 to 8 years	800 mg
9 to 18 years	1300 mg
19 to 50 years	1000 mg
51 years and older	1200 mg

Natural dietary sources of calcium include dairy products (milk, cheese, yogurt), dark leafy vegetables such as spinach and broccoli, and tree nuts such as almonds and pecans. Many foods sold in the United States are calcium-fortified (contain added calcium). They include orange juice, cereals, breads, SOY milk, and soy products such as tofu. Low-fat dairy products, which have lower amounts of saturated fats, are the more healthful choice and contain just as much calcium as higher fat products. Labels on packaged foods in the United States state, per serving, the food's calcium

DIETARY SOURCES OF CALCIUM

Food Source	Serving Size	Amount of Calcium per Serving
almonds	3 ounces	210 milligrams (mg)
blackstrap molasses	1 tablespoon	170 mg
bok choy (cooked)	1 cup	160 mg
broccoli (cooked)	1 cup	60 mg
canned salmon (with bones)	3 ounces	180 mg
canned sardines (with bones)	3 ounces	325 mg
clams (steamed)	3 ounces	80 mg
collards	1 cup	265 mg
cottage cheese	1 cup	155 mg
crab (steamed)	3 ounces	90 mg
hard cheese (cheddar, swiss)	1 ounce	225 mg
kale (cooked)	1 cup	95 mg
milk	1 cup	300 mg
mollusks (steamed)	3 ounces	80 mg
mozzarella cheese	1 ounce	200 mg
okra	1 cup	125 mg
provolone cheese	1 ounce	205 mg
raisins	1 cup	75 mg
rhubarb (cooked)	1 cup	345 mg
ricotta cheese	½ cup	335 mg
sauerkraut	1 cup	70 mg
spinach (cooked)	1 cup	245 mg
turnip greens (cooked)	1 cup	200 mg
yogurt	8 ounces	425 mg

content and its percentage of the daily adequate intake (AI) amount.

Three forms of calcium are commonly available as dietary supplements: calcium carbonate, calcium citrate, and calcium phosphate. However, many doctors believe the form of calcium matters far less than maintaining adequate intake of calcium. Individuals have varying tolerances and responses to the different forms of calcium supplements. Many doctors recommend calcium carbonate in the form of chewable antacid tablets as the most available, easiest to take, and least expensive calcium supplement product. Because numerous factors influence how much calcium the gastrointestinal tract absorbs, health experts recommend obtaining as much calcium as possible through dietary sources with calcium supplementation to make up the difference. Total calcium consumption that exceeds 2000 milligrams (mg) a day does not provide any added benefit and may cause health problems due to excessive calcium.

The body also requires vitamin D to absorb dietary calcium. The primary sources of vitamin D are sunlight and dietary supplements. The body can synthesize (make) as much vitamin D as it needs with adequate SKIN exposure to sunlight. However, many people do not get enough sunlight. SUN PROTECTION products, necessarily applied to protect against SUNBURN block the ultraviolet rays that activate vitamin D synthesis. As well, there is not adequate ultraviolet light exposure during the winter months for people who live in the northern hemisphere—in the United States, above a line roughly drawn from San Francisco to Boston. Because of these factors, most calcium-fortified foods also contain supplemental vitamin D. Inadequate vitamin D causes softness of the bones—RICKETS in children and OSTEOMALACIA in adults—regardless of calcium intake because the body cannot absorb calcium without vitamin D.

Though insufficient calcium intake is by far the more significant health issue because of the effect it has on bones, excessive calcium consumption has potentially serious adverse effects on the body systemically. Excessive calcium can cause ARRHYTHMIA (irregularity in the HEART RATE), MUSCLE cramps, kidney stones (NEPHROLITHIASIS), and NERVE disturbances.

See also CRAMP; DIET AND HEALTH; EXERCISE AND HEALTH; HYPERCALCEMIA; HYPERPARATHYROIDISM; HYPOCALCEMIA; HYPOPARATHYROIDISM; MINERALS AND HEALTH; PARATHYROID GLANDS; SMOKING AND HEALTH; VITAMINS AND HEALTH.

carpal tunnel syndrome A collection of symptoms resulting from compression of the median NERVE as it passes through the carpal tunnel, a narrow channel in the carpal bones of the wrist. The ligaments that form the carpal tunnel can become irritated and inflamed, constricting the median nerve and the tendons in the area. The median nerve supplies the inside of the hand, the thumb, and the first three fingers (the ulnar nerve supplies the outside of the hand and the little finger). Compression of the nerve affects sensation and function in the hand.

Symptoms and Diagnostic Path

Symptoms of carpal tunnel syndrome progress gradually over months to years. They may include

- tingling
- numbness
- weakness
- loss of ability to use the thumb and first two or three fingers
- PAIN that shoots from the hand up the forearm

Some people also experience perceptible swelling and tenderness to touch over the wrist. Symptoms are generally intermittent at the onset and progress to occur more frequently and have greater intensity. The diagnostic path includes tests of the hand and wrist that are able to bring on or intensify the symptoms. The doctor may order electromyogram (EMG) and nerve conduction studies for further diagnostic information.

Treatment Options and Outlook

Treatment efforts attempt to manage symptoms conservatively, with measures such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), injection of a corticosteroid, and splinting. When fluid retention (edema) is a factor, diuretic medications ("water pills") may help. Some people experience

improvement in their symptoms when they take vitamin B_6 (pyridoxine) supplements. Certain YOGA postures that increase FLEXIBILITY and STRENGTH of the wrists improves symptoms for some people. Surgery, either open or laparoscopic, to cut the carpal LIGAMENT is the curative treatment for most people who have carpal tunnel syndrome. Such an OPERATION opens the carpal tunnel, relieving compression against the median nerve. Full recovery from the open procedure takes about 12 weeks and from the laparoscopic procedure about 8 weeks. A rare complication of carpal tunnel surgery is permanent weakness in the hand as a consequence of cutting the median nerve. Other possible complications, also rare, include excessive bleeding and postoperative INFECTION.

Risk Factors and Preventive Measures

Doctors believe many people who develop carpal tunnel syndrome have an inherently narrow carpal tunnel, making the passage tighter. Women, who have smaller BONE structures than men, are three times more likely to develop carpal tunnel syndrome. Carpal tunnel syndrome may also follow injury to the wrist, such as strain or FRACTURE, or accompany OSTEOARTHRITIS of the wrist. People who have DIABETES, PERIPHERAL VASCULAR DISEASE (PVD), and other conditions associated with NEUROPATHY (injury to the nerves) are particularly susceptible to compression syndromes such as carpal tunnel syndrome.

Work that subjects the wrists to continuous vibration or repetitive movement also increases the risk for carpal tunnel syndrome. The highest risk is among people who do assembly-line work, such as in manufacturing, professional sewing, meat packing, and poultry processing. Job tasks in these occupations subject the wrists to repeated flexing under pressure. Though occupations involving extensive typing, keyboarding, or data entry were long suspected as prime causes of carpal tunnel syndrome, recent studies support only a slight increase in risk. Frequent short breaks to stretch and flex the wrists during work and wearing supportive wrist braces can help prevent carpal tunnel syndrome or minimize its symptoms.

See also ENDOSCOPY; OCCUPATIONAL HEALTH AND SAFETY; REPETITIVE MOTION INJURIES; SPRAINS AND STRAINS; SURGERY BENEFIT AND RISK ASSESSMENT; TENDON.

cartilage Dense connective tissue that provides the foundation for BONE in the developing fetus and covers bone ends in the joints in adults. The fetal SKELETON forms first as a translucent type of cartilage called hyaline cartilage, with conversion to bone beginning at about the fourth week of pregnancy. Calcification continues after birth. In the adult skeleton, hyaline cartilage forms the disks between the vertebrae in the back, the rings that give the TRACHEA stability, and the extensions that connect the ribs to the sternum. A type of cartilage that contains fibers of elastin that allow greater FLEXIBILITY, called elastic cartilage or yellow cartilage, gives shape to the outer ears (auricles), auditory canal (EAR canal), and end of the NOSE.

Cartilage consists of a thick, somewhat elastic base of collagen (an insoluble protein) with small clusters of cartilage cells (chondrocytes) suspended within it. Though cartilage does not have its own BLOOD or NERVE supplies, it continuously renews itself through a process called remodeling in which chondrocytes facilitate a slow turnover of collagen molecules and other substances. This remodeling provides chondrocytes with the NUTRIENTS they need to function.

Researchers believe imbalances in the remodeling process, in which the breakdown of collagen molecules exceeds rebuilding, is the basis for OSTEOARTHRITIS. Various mechanisms, notably repeated trauma such as through use of the joints and activation of CYTOKINES through the inflammatory process, contribute to this imbalance. Damage to cartilage is the foundation of osteoarthritis, HERNIATED NUCLEUS PULPOSUS, and most KNEE INJURIES.

For further discussion of cartilage within the context of musculoskeletal structure and function, please see the overview section "The Musculoskeletal System."

See also BURSA; JOINT; LIGAMENT; TENDON.

cervical spondylosis Narrowing of the channel between the vertebrae in the neck through which the SPINAL CORD passes. Cervical spondylosis results from chronic, degenerative OSTEOARTHRITIS in which there is extensive INFLAMMATION and damage to the CARTILAGE disks that separate and cushion the cervi-

cal vertebrae (bones of the neck). The damage is permanent and eventually restricts the movement of the neck. Pressure against the NERVE roots of the spinal cord may cause tingling or loss of sensation in the shoulders and arms. Sometimes the pressure also causes weakness of the muscles in the upper back and the arms. Cervical spondylosis is more common in people over age 60.

Symptoms of cervical spondylosis include

- stiffness in the neck
- HEADACHE
- PAIN along the back of the neck that radiates into the shoulders and upper arms
- abnormal sensation in the upper back and arms, sometimes extending to the hands and fingers

The diagnostic path includes X-RAY of the neck and upper back, which typically reveals the changes in the alignment of the vertebrae as well as the formation of bone spurs and calcifications within the disks. Additional imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), and myelogram (injection of radio-opaque dye into the spinal column) often show the degree to which the spondylosis compresses the nerve roots or, when degeneration is severe, the spinal cord itself.

Treatment options include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve inflammation and pain. A soft cervical collar that immobilizes the neck allows the muscles of the neck to relax, helping inflammation to recede. Injections of steroid medications can often reduce inflammation that does not respond to other treatments. Heat and PHYSICAL THERAPY aid HEALING and restoration of movement. Though cervical spondylosis is a chronic and progressive condition, most people are able to obtain relieve through a combination of medical and lifestyle methods.

See also ANKYLOSING SPONDYLITIS; BACK PAIN; BONE SPUR; CHRONIC PAIN; LIFESTYLE AND HEALTH.

Charcot-Marie-Tooth (CMT) disease An inherited neuromuscular disorder in which the myelin sheath that covers and protects the PERIPHERAL NERVES deteriorates. The loss of the myelin sheath allows NERVE signals to escape from the nerves before they reach their destinations. CMT is the most common inherited neuromuscular disorder in the United States, affecting about 150,000 Americans. CMT is slowly progressive though not fatal, with symptoms typically beginning in late ADOLESCENCE or early adulthood.

There are numerous forms of CMT, each arising from MUTATION of different genes that encode the proteins that form the myelin sheath. The most common is CMT1, which occurs in three autosomal dominant variations that cause abnormal structure in the myelin sheath:

- CMT1A results when the person inherits an extra copy of the GENE on CHROMOSOME 17 that encodes peripheral myelin protein 22 (PMP-22), causing excessive production of PMP-22.
- CMT1B occurs as a result of mutations to the gene that encodes myelin protein 0 (MP-0).
- CMT1C results from mutations to genes that encode for other peripheral myelin proteins, though researchers have not yet identified the mutations.

Other forms of CMT include

- CMT2, in which there are defects in the axons of the peripheral nerves rather than in the structure of the myelin sheath
- CMT3, also called Dejerine-Sottas disease, which results from mutations to the MP-0 or PMP-22 gene and causes severe symptoms beginning in the first year of life
- CMT4, in which various gene mutations cause symptoms that begin in childhood and progress to complete loss of motor function of the lower extremities by adolescence
- CMTX, which arises from a mutation in the connexin 32 gene on the X chromosome and causes more severe symptoms in males

Occasionally CMT occurs as a spontaneous mutation, without family history of the disease, and may affect any of the genes that encode for myelin proteins.

Symptoms and Diagnostic Path

Symptoms affect primarily the legs and feet in most forms of CMT, though in some forms may

also affect the arms and hands. Though the motor symptoms of CMT are most prominent, CMT also affects sensory perceptions and can cause tingling and numbness (PARESTHESIA). Characteristic symptoms of CMT include

- apparent clumsiness or difficulty walking, running, and jumping
- progressive weakness in the legs and feet, and occasionally in the arms and hands
- atrophy (wasting) of MUSCLE mass in the affected extremities
- diminished sensory perception in the extremities, particularly of heat, cold, and PAIN
- foot drop and heel slap when walking, indications of muscle weakness in the lower leg and foot

The diagnostic path includes a comprehensive NEUROLOGIC EXAMINATION, detailed PERSONAL HEALTH HISTORY, nerve conduction studies, and electromyogram (EMG). The neurologist may also perform a nerve biopsy to examine the structure of nerve cells in the muscle tissue and GENETIC TESTING for mutations known to cause CMT. The neurologic examination typically shows diminished or absent reflexes at the elbow, knee, and ACHILLES TENDON.

Treatment Options and Outlook

CMT is a progressive, lifelong condition. Symptoms in CMT1 generally stop short of complete loss of motor function in the affected extremities. Other forms of CMT, notably CMT4 and CMTX, may result in inability to walk. PHYSICAL THERAPY and daily physical activity—STRENGTH exercise, RESISTANCE EXERCISE, and activities to improve balance and FLEXIBILITY such as YOGA—can extend unassisted mobility. Bicycling and swimming are excellent activities for AEROBIC EXERCISE as well as for strengthening and flexibility with minimal impact on the ankles, which are the most vulnerable as CMT progresses. Adaptive devices such as braces, walkers, and wheelchairs can aid mobility when motor function deteriorates to a point that cannot support independent mobility. Some people benefit from surgery to rebalance muscles and tendons, in particular to provide support for the feet. Despite the progressive nature of CMT, the condition is not fatal; and with adaptive devices and environmental modifications, most people who have CMT can enjoy productive lifestyles.

Risk Factors and Preventive Measures

CMT is nearly always an inherited condition, so the key risk factor is genetics. GENETIC COUNSELING can assist couples with FAMILY PLANNING. Early diagnosis and treatment preserves muscle strength and function to the greatest extent possible. High-top shoes and braces to support the ankle extend mobility and reduce the risk for ankle injuries such as sprains, strains, and fractures.

See also DISABILITY AND EXERCISE; EXERCISE AND HEALTH; FRACTURE; GENETIC DISORDERS; INHERITANCE PATTERN; REFLEX; SPRAINS AND STRAINS.

Charcot's joints See NEUROGENIC ARTHROPATHY.

chondritis INFLAMMATION of CARTILAGE that may occur anywhere in the body though is most common in the cartilage of the ribs (costochondritis), on the ends of the bones (osteochondritis), and within the external EAR (auricular chondritis). Chondritis often results from trauma, such as a blow or, when the external ear is involved, after a burn injury. Bacterial INFECTION may accompany the inflammation. Polychondritis is an autoimmune disorder in which inflammation affects multiple locations of cartilage throughout the body. Some rheumatologists believe polychondritis is a form of VASCULITIS. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) may suppress the inflammatory response. Bacterial infection requires treatment with ANTIBIOTIC MEDICATIONS. However, chondritis may respond slowly to treatment because cartilage does not have a BLOOD supply to carry medications to the site of the inflammation. Heat and rest may provide some relief.

See also AUTOIMMUNE DISORDERS; BACTERIA; SYNOVITIS; TENDONITIS.

clubfoot See TALIPES EQUINOVARUS.

congenital hip dysplasia A condition in which the head of the femur (thigh BONE) does not properly seat in the acetabulum (pelvic socket) at birth. Numerous potential causes may account for

congenital hip DYSPLASIA, also called congenital hip displacement or developmental dysplasia of the hip. The dysplasia is sometimes apparent at birth; doctors may suspect it when the delivery presentation is breech because this holds the infant's hips in a flexed position. Symptoms may include a perceptible clicking, often felt and heard, when moving the legs to activate the hip JOINT. Rarely, the leg may be obviously out of alignment with the pelvis. X-RAY can often confirm the diagnosis, though some dysplasias may not be detectable until the infant is older.

The pediatrician may choose watchful waiting for a mild dysplasia. A special brace called a Pavlik harness holds the hips in their proper position in moderate dysplasia, until the connective tissues develop the STRENGTH to hold the femur snugly within the acetabulum. Severe dysplasia or dysplasia that is undetected until the child is walking may require closed reduction, in which the orthopedic surgeon manipulates the joint into place with the child under ANESTHESIA, or open reduction, in which the orthopedic surgeon makes surgical repairs to the joint. Early and appropriate treatment is important for proper mobility and development of the leg.

See also BIRTH DEFECTS; CONGENITAL ANOMALY; SURGERY BENEFIT AND RISK ASSESSMENT.

contracture An abnormal shortening or tightening of connective tissue or MUSCLE that impedes proper movement of a JOINT, digit, or other musculoskeletal structure. Contractures typically develop when fibrous tissue (scarring), which is relatively inflexible, replaces normal connective tissue. This process may reflect autoimmune activity in the body (such as occurs in RHEUMATOID ARTHRITIS), repeated trauma (such as occurs in REPETITIVE MOTION INJURIES), or a neuromuscular disorder (such as MUSCULAR DYSTROPHY or CEREBRAL PALSY). Contractures can cause permanent deformity of joints, resulting in limited function or movement.

Common types of contracture include

- Dupuytren's contracture, in which fibrous tissue in the fascia of the hand causes the ring and sometimes little (third and fourth) fingers to draw toward the palm
- foot drop, which results from damage to the muscles and nerves of the lower leg
- wrist drop, which results from damage to the muscles and nerves of the lower arm
- Volksmann's contracture, which results from injury that restricts the flow of BLOOD to the forearm and hand

Early symptoms of contracture include difficulty straightening a joint and occasionally discomfort or PAIN with movement of the joints. Therapeutic efforts such as gentle stretching and braces may improve function, though surgery may be necessary to release fibrotic tissue.

See also ARTHROGRYPOSIS; SCAR; TALIPES EQUINOVARUS.

cramp A painful, involuntary, and often extended contraction of a MUSCLE. Cramps may occur in any muscle and often occur with overuse, such as writer's cramp and leg cramps during running. Overexertion, DEHYDRATION, and fatigue are key contributors to muscle cramps. Uterine cramps are common with MENSTRUATION. Gentle stretching and massage can relieve the contraction, allowing the muscle to relax. Heat to the area, such as with menstrual cramps, helps maintain the muscle in a relaxed state. Stretching before physical exercise helps prepare the muscles for activity. Adequate hydration helps muscles release toxic byproducts into the BLOOD circulation.

See also DYSMENORRHEA; SPASM.

crepitus A cracking, clicking, or snapping sound, also called crepitation, that occurs with movement of a JOINT. Crepitus may occur in normal, healthy joints though is often quite pronounced in degenerative joint disorders in which the surfaces of joint structures are rough or irregular and protective CARTILAGE structures have deteriorated. Crepitus is a common feature of TEMPOROMANDIBULAR DISORDERS, PATELLOFEMORAL SYNDROME, fractures due to trauma, and OSTEOARTHRITIS.

See also FRACTURE; RHEUMATOID ARTHRITIS.

D–G

dislocations Separations of the structures within a JOINT, typically as a result of traumatic injury. The digits (fingers and toes), shoulders, and hips are particularly vulnerable to dislocation. Traumatic dislocation is very painful. Generally a doctor should reduce the dislocation (restore the bones to their correct positions) and evaluate the injury for any damage that would require additional treatment; however, people tend to "pop" dislocations back into place themselves. Such self-treatment can cause further trauma, depending on the circumstances. Splinting the joint and applying ice to the area can reduce swelling and PAIN until the doctor can realign the structures. Sometimes a dislocation reflects an abnormality of the joint that requires a doctor's assessment and treatment to prevent subsequent dislocations.

See also FRACTURE; RICE; SPRAINS AND STRAINS.

dwarfism See SKELETAL DYSPLASIA.

dystonia Extended contractions of the muscles that hold the body in unnatural postures. Dystonia may occur as a primary disorder of movement, typically a hereditary disorder, or as an undesired SIDE EFFECT of certain medications to treat PARKINSON'S DISEASE, PSYCHOSIS, SCHIZOPHRENIA, and SEIZURE DISORDERS that affect DOPAMINE binding in the BRAIN. Dopamine is a key NEUROTRANSMITTER for movement as well as for mood. Sometimes, though unfortunately not always, stopping the medication ends DRUG-related dystonia. Inherited forms of primary dystonia may be spastic (involve rigid, distorted postures) or repetitious, often rhythmic, involuntary movements such as grimaces, twitches, and jerking.

There are no treatments for primary dystonia that are certain to stop the MUSCLE contractions. Some people experience relief with high doses of anticholinergic drugs that affect acetylcholine, a neurotransmitter important to fine motor movements. When the dystonia occurs in a localized or regional part of the body, BOTULINUM THERAPY (injections of weakened botulinum toxin) sometimes can paralyze the muscles enough to significantly reduce or eliminate the dystonia. The effects of botulinum therapy are temporary, however, with repeat treatments required about every six months.

See also BLEPHAROSPASM; SPASM; TIC; TORTICOLLIS.

epicondylitis INFLAMMATION of the TENDON at the elbow end of the humerus (long BONE of the upper arm). Epicondylitis may be lateral or medial. Lateral epicondylitis, commonly called tennis elbow, affects the outer side of the elbow (little finger side). Bending the wrist back or applying pressure to the bony projection (the humeral epicondyle) on the outside of the elbow causes PAIN at the elbow. Painting and plastering are common occupational causes of lateral epicondylitis. Medial epicondylitis, commonly called baseball elbow or golfer's elbow, affects the inner side of the elbow (thumb side). Bending the wrist toward the palm of the hand or squeezing a ball held in the palm of the hand causes pain at the base of the elbow.

The doctor makes the diagnosis on the basis of symptoms and personal history of overuse or a blow to the elbow. Diagnostic procedures are usually not necessary. Treatment combines NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) or injections of CORTICOSTEROID MEDICATIONS, which reduce inflammation and pain, with alternating heat and cold to the area. A brace or band worn over the humeral epicondyle provides relief for some people. Epicondylitis generally goes away in

8 to 12 weeks. Recurrent epicondylitis may require surgical repair.

See also OSTEOARTHRITIS; TENDONITIS.

fascia The fibrous membrane that covers connective tissue. Deep fasciae enclose, support, and separate MUSCLE structures deep within the body. Superficial fasciae support the SKIN and connect the skin to inner layers of tissue. Fascia has high tensile STRENGTH and a sheetlike appearance. It varies in thickness, depending on its location and purpose. Fasciae throughout the body are susceptible to INFECTION, INFLAMMATION, and traumatic injury.

See also CONTRACTURE; FIBROMYALGIA NECROTIZING FASCIITIS; PLANTAR FASCIITIS.

fibromyalgia A chronic condition of PAIN felt in the muscles and connective tissues throughout the body, with accompanying fatigue and multiple trigger points (areas on the body where the slightest touch activates a severe pain response). Characteristically people experience a constant level of discomfort with pressure or contact causing overt pain in the shoulders, chest, back, hips, and knees. Many people also experience stiffness in the areas of pain, similar to the stiffness of RHEUMATOID ARTHRITIS or OSTEOARTHRITIS. However, there is no JOINT INFLAMMATION or deterioration with fibromyalgia. Fibromyalgia may persist for months to years. About 6 million Americans have fibromyalgia, the majority of whom are women. Researchers believe fibromyalgia develops through a convergence of multiple factors.

Symptoms and Diagnostic Path

The symptoms of fibromyalgia are widely variable, making diagnosis somewhat of a challenge for many people. Some people have periods of weeks to months without any symptoms, interlaced with periods of weeks to months with symptoms severe enough to prevent normal activity. Other people have a clear path of symptom onset, persistence, and improvement that spans months to years. Characteristic symptoms of fibromyalgia include

- MUSCLE pain throughout the body
- sleep disturbances such as insomnia and RESTLESS LEGS SYNDROME
- fatigue
- gastrointestinal symptoms that suggest IRRITABLE BOWEL SYNDROME (IBS), such as frequent NAUSEA and DIARRHEA
- DEPRESSION, anxiety, and mood swings
- headaches
- hypersensitivity to sensory stimulation (sight, sound, touch, taste, smell)

The diagnostic path begins with a comprehensive medical examination including general BLOOD and urine tests, a NEUROLOGIC EXAMINATION, and detailed PERSONAL HEALTH HISTORY. The doctor may conduct further tests to rule out other conditions that can cause similar symptoms, such as rheumatoid arthritis and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). However, there are no tests that can confirm the diagnosis of fibromyalgia. Doctors typically follow clinical guidelines for reaching a diagnosis of fibromyalgia that include the presence of these key signs:

- diagnostic tests rule out other possible causes for the symptoms
- point tenderness (discomfort or pain with mild pressure) at a minimum of 11 places on the body
- widespread, persistent aching or pain in the muscles and joints for at least three months

The diagnosis also considers factors researchers believe may be precipitating, such as recent INFECTION or injury, the existence of any AUTOIMMUNE DISORDERS, and family history of fibromyalgia. Symptoms generally begin between ages 30 and 50.

Treatment Options and Outlook

Treatment efforts focus on relieving symptoms to a degree that allows participation in regular activities and satisfactory QUALITY OF LIFE with the presumption that symptoms will persist indefinitely. Though the condition may eventually go away, in most people the course of fibromyalgia is unpredictable though symptoms do not worsen. Treatment is a process of finding the combination of approaches that most effectively relieves symptoms. Common treatment options include

- ANALGESIC MEDICATIONS such as acetaminophen and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve pain
- ANTIDEPRESSANT MEDICATIONS to treat depression and to relieve pain
- MUSCLE RELAXANT MEDICATIONS
- CHIROPRACTIC, OSTEOPATHIC MANIPULATIVE TREATMENT (OMT), and MASSAGE THERAPY to relax muscles and improve range of motion and FLEXIBILITY of joints
- ACUPUNCTURE for pain relief and stress reduction
- YOGA and TAI CHI to improve flexibility, STRENGTH, and balance and to relieve stress
- MEDITATION for stress relief

Doctors seldom prescribe narcotic pain relievers, sleep medications, CORTICOSTEROID MEDICATIONS (such as prednisone), or benzodiazepine muscle relaxants (such as diazepam), because these treatments interfere with normal activities and are not proven to improve symptoms long term. As well, the side effects and potential dependency issues with these medications are greater than the short-term benefits for most people. Doctors also recommend daily physical exercise because it increases the release of endorphins and enkephalins, the body's natural pain relievers. It also stretches and strengthens the muscles and connective tissues, and promotes a sense of accomplishment and well-being.

Risk Factors and Preventive Measures

About 80 percent of people who have fibromyalgia are women, though researchers do not know why this gender correlation exists. People who have autoimmune forms of arthritis, such as rheumatoid arthritis or ANKYLOSING SPONDYLITIS, also have increased risk for fibromyalgia. Because researchers do not know what causes fibromyalgia, there are no recommended preventive measures.

See also ACUTE PAIN; ALTERNATIVE METHODS FOR PAIN RELIEF; CHRONIC FATIGUE SYNDROME; CHRONIC PAIN; STRESS AND STRESS MANAGEMENT.

fracture A break in a BONE. The most common cause of bone fracture is traumatic injury. Spontaneous fracture may occur in people who have health conditions such as OSTEOGENESIS IMPERFECTA, severe OSTEOPOROSIS, or BONE CANCER. Fractures may take various forms, including

- avulsion, in which a small chip of bone breaks away
- closed (simple), in which the bone ends remain relatively in alignment and do not penetrate through the SKIN
- comminuted, in which the bone fragments into multiple pieces
- compression, in which the bones collapse onto one another (such as vertebrae in the back)
- greenstick, which typically occur in young children whose bones are still supple and appear as a bend or curve rather than an outright break in the bone
- open (compound), in which the bone ends are significantly separated and protrude through the skin, causing an open wound
- spiral, which occur when sudden force twists the bone and the break runs in line with the bone's axis
- stress, in which hairlike cracks develop in bones subject to repetitive stress (such as the tibia, the long bone in the lower leg, with running)

Bone fractures require prompt care from a doctor. Nearly always it is necessary to immobilize the bone ends so they remain aligned and can heal back together.

Do NOT move a person who may have a fractured neck or back. Summon emergency medical aid and keep the person still, calm, and as comfortable as possible.

Symptoms and Diagnostic Path

Severe PAIN and rapid swelling after trauma are the most common symptoms of bone fracture. Most often, the person cannot bear weight or put pressure on the involved area. The limb or digit may appear distorted or a bone end may protrude through the skin. X-RAY nearly always confirms the diagnosis, though more sophisticated imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and bone scan are occasionally necessary

to confirm stress fractures and some spiral fractures.

Treatment Options and Outlook

Treatment immobilizes the bone ends. The most common method of immobilization is a plaster or fiberglass cast, applied as a wet wrap around the fracture and usually spanning the joints above and below the break in the bone. The cast hardens as it dries, and remains in place for three to six weeks for most fractures. Other methods of external immobilization include splints and braces.

Sometimes the doctor must move the bone ends into alignment, a procedure called reduction. For most fractures that require reduction, the doctor first administers a strong sedative or ANESTHESIA, then manipulates the bones. When no incision is necessary the reduction is a closed reduction; when the doctor must open the fracture site to realign the bones the reduction is an open reduction (surgery). During an open reduction the doctor generally places pins, plates, screws, or nails to hold the bone ends in place. Fractures set via open reduction generally do not require casting and the person can return to movement as tolerated because the hardware holds the bone together.

Most fractures heal within 6 to 10 weeks. Immobilized muscles atrophy (shrink), and the person may need PHYSICAL THERAPY to restore MUSCLE STRENGTH and JOINT range of motion after the doctor removes the cast or other immobilizing device. The area of HEALING remains thicker than the rest of the bone for up to a year. Refracture at the same site is very unlikely.

Risk Factors and Preventive Measures

MOTOR VEHICLE ACCIDENTS and athletic or recreational activities that expose a person to impact or falling present the greatest risk for fractures. Older people are vulnerable to fractures with falls, primarily as a consequence of OSTEOPENIA or osteoporosis (conditions in which the bones become thin and weak). Proper protective equipment—for example seat belts, pads, braces, and helmets—can prevent many fractures and other injuries.

See also ACCIDENTAL INJURIES; ATHLETIC INJURIES; CONCUSSION; HIP FRACTURE IN OLDER ADULTS; SPRAINS AND STRAINS.

frozen shoulder See ADHESIVE CAPSULITIS.

gangrene The death of tissue (necrosis) resulting from deprivation of BLOOD circulation to an area of the body. Gangrene most commonly affects the digits (fingers and toes) and extremities (hands and feet). FROSTBITE, PERIPHERAL VASCULAR DISEASE (PVD), NEPHROPATHY of DIABETES, severe INFECTION (such as clostridial infections and NECROTIZING FASCIITIS), and RAYNAUD'S SYNDROME are common causes of gangrene. TESTICULAR TORSION in which a TESTICLE becomes strangulated (twisted such that its blood supply is cut off) can result in testicular gangrene. A strangulated HERNIA, which entraps a segment of bowel, can similarly result in intestinal gangrene. Gangrene can also affect internal organs that lose their blood supply, such as may occur with a major thromboembolism (blood clot in an ARTERY). Gangrene tends to progress as it consumes healthy tissue. Gangrenous tissue is characteristically black or greenish black and may have a foul odor. Because the tissue is dead, the person has no sensation of PAIN from the area though inflamed tissue at the periphery of the gangrenous tissue may cause intense pain.

Methods to improve blood circulation, such as thrombolytic medications to dissolve blood clots and vasodilator medications to dilate (widen) the arteries for increased blood flow, may restore enough circulation to allow the area to heal. Oxygen delivered under pressure in a hyperbaric chamber is sometimes successful in restoring enough oxygen to the tissues that they can begin to heal. Generally, however, the doctor must surgically remove all gangrenous tissue for HEALING to take place. Such removal may require AMPUTATION of the affected digit or limb. Often recovery is then complete, depending on the underlying cause for the gangrene. People who have diabetes, PVD, or peripheral neuropathy have increased risk for gangrene to develop in what would otherwise be minor wounds.

See also INFECTIOUS ARTHRITIS; OSTEOMYELITIS; PROSTHETIC LIMB.

gout A form of inflammatory arthritis. Gout develops when uric acid crystals form within the JOINT capsules, causing irritation and INFLAMMATION. Uric acid is a waste byproduct of the METABOLISM of

forms of protein (nucleic acids) called purines. Purines occur naturally in the body as well as in meats consumed in the diet (especially organ meats such as liver and fish such as mackerel and herring). The most common site for gout is the first (largest) joint of the big toe. Gout may also affect the metatarsal and tarsal joints in the feet as well as the ankles and knee; it less commonly involves the fingers and wrists.

Symptoms and Diagnostic Path

Gout generally begins with sudden and severe PAIN in the affected joint, usually the first joint of the big toe. The pain commonly arrives at night and wakes the person. The affected joint may be red, swollen, and warm to the touch. The pain and other symptoms typically go away within 10 days, and there can be an extended period before symptoms return. The diagnostic path includes X-rays of the affected joints and tests of the BLOOD and URINE to measure uric acid levels. Sometimes the doctor will numb the joint and use a needle and syringe to withdraw synovial fluid to examine for the presence of uric acid crystals. As gout progresses, often the uric acid crystals also form deposits, called tophi, under the SKIN.

Treatment Options and Outlook

Treatment during a gout attack focuses on relieving inflammation and pain. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NASAIDS) or CORTICOSTEROID MEDICATIONS are generally the first line of medications to target these symptoms. Medications to reduce the risk for future gout attacks include colchicine, allopurinol, and probenecid, which slow the body's production of uric acid. These medications do not prevent gout from progressing but can extend the time between attacks as well as reduce the permanent damage the inflammation can cause.

FOODS WITH HIGH PURINE CONTENT

anchovies	asparagus	bacon
beef	beer	brains
cod	crab	duck
ham	herring	kidneys
lentils	liver	lobster
mackerel	mushrooms	mussels
oysters	sardines	scallops
shrimp	sweetbreads	trout
turkey	veal	venison

Risk Factors and Preventive Measures

About 20 percent of people who have gout also have other family members who have gout, giving rise to suspicion of a genetic factor. Circumstances that increase the amount of uric acid in the blood circulation significantly raise the risk for gout. Such circumstances include consumption of foods high in purines, medications that affect the body's ability to excrete purines (such as diuretic medications and immunosuppressive drugs after ORGAN TRANSPLANTATION), DIABETES, HYPERLIPIDEMIA, and OBESITY. Excessive ALCOHOL consumption interferes with the ability of the KIDNEYS to filter uric acid from the blood. Though there do not appear to be effective ways to prevent gout from developing, avoiding circumstances that increase blood uric acid levels can reduce the frequency and severity of gout attacks. Men are more likely to develop gout before age 50 and women after age 50.

See also OSTEOARTHRITIS; RHEUMATOID ARTHRITIS.

hernia A separation or tear in the fibers of a MUSCLE that allows the underlying tissue or structure to bulge through. Hernias may occur as a result of congenital weakness or incomplete closure of a channel in the muscle (such as an umbilical or inguinal hernia) or because of injury (unintended or surgical). The common types of hernia are

- inguinal hernia, which occurs in the inguinal canal (groin)
- femoral hernia, which occurs in the upper thigh
- umbilical hernia, which occurs at the umbilicus (belly button)
- HIATAL HERNIA, which occurs in the DIAPHRAGM and is not visually perceptible
- incisional hernia, which occurs at the site of a surgical incision, usually abdominal

Hernias present in children often heal as the child grows. Hernias in adults are often present from childhood and become problematic when some sort of strain puts pressure on them. Hernias are somewhat more common in men. When the person or doctor can push the hernia back into the muscle wall it is reducible; an incarcerated hernia is a hernia that will not recede. When the hernia traps a segment of intestine or other tissue to the extent that it cuts off the BLOOD supply, it is a strangulated hernia. Though some hernias, particularly in children, may correct themselves, most hernias require surgery to repair the defect in the muscle wall.

Symptoms and Diagnostic Path

A hernia may appear as a painless bulge or may cause discomfort, depending on its location and the extent to which it allows intestinal structure to protrude through the muscle wall. Many abdominal hernias are more prominent with coughing or bearing down. Symptoms of hiatal hernia may include DYSPEPSIA (heartburn) and difficulty swallowing. Diagnosis is primarily clinical, based on the appearance of the symptoms. The doctor may request an ULTRASOUND examination to confirm the presence of the hernia and to create a visual image to help assess the appropriate therapeutic course.

Treatment Options and Outlook

Most hernias require surgery to repair the weakness in the muscle wall. The doctor may decide to take an approach of watchful waiting when the hernia is very small, in a young child, or in a person for whom surgery is a significant risk. Nonsurgical approaches such as a truss (a supportive device that places pressure against the hernia to keep it within the abdominal wall) may relieve symptoms for the short term but cannot correct the hernia. Though some hernias may remain small and inconsequential for long periods of time they may become problematic without warning, at which point they may require immediate or urgent medical attention. An incarcerated hernia is a medical emergency that requires immediate surgery, otherwise the strangulated tissue dies and is at very high risk for GANGRENE.

Hernia repair surgery, called herniorrhaphy or hernioplasty, can be OPEN SURGERY (an OPERATION in which the surgeon makes a two- to three-inch-long incision over the site of the hernia and directly exposes the involved muscles) or MINIMALLY INVASIVE SURGERY (an operation in which the surgeon uses a laparoscope and special instruments to operate through one to three small incisions). ANESTHESIA may be regional, epidural, or

general. Variables that influence the surgeon's decision about the type of operation include the location and size of the hernia, the person's age and general health status, and whether the hernia is reducible or incarcerated.

For most hernia repairs the surgeon places a small piece of plastic mesh behind the opening in the muscle wall to help support the muscle layers. The surgeon then sutures those layers together to restore stability and STRENGTH to the muscle wall. Recovery takes about two weeks for a laparoscopic surgery and up to six weeks for an open surgery. Once repaired, hernias do not generally recur though it is common to feel twinges of discomfort and even PAIN periodically at the site up to several years after the surgery.

Risk Factors and Preventive Measures

Repeated straining, such as with bowel movements or because of chronic COUGH, can pressure a weak place in the abdominal wall. Though sudden, strenuous movement can bring out a hernia, such movement can occur with a strong SNEEZE or cough as easily as lifting too heavy a weight. Regardless of the activity that bears blame, the underlying cause of a hernia is a weakness in the muscle structure. Though exercises to improve muscle strength may prevent injuries such as strains and muscle tears, exercises cannot prevent or treat hernia. There are no known measures for preventing hernia.

See also SURGERY BENEFIT AND RISK ASSESSMENT; SWALLOWING DISORDERS.

herniated nucleus pulposus Damage to the structure of the CARTILAGE that cushions the vertebrae, also called a herniated, slipped, or ruptured disk. A herniated nucleus pulposus becomes increasingly common with advancing age, the result of wear and deterioration of the tough outer cartilage (called the annulus fibrosus) that allows the soft inner portion of the disk (called the nucleus pulposus) to bulge beyond its enclosure. Often there is a clear tear in the outer cartilage (a rupture). A traumatic injury, such as a motor vehicle accident, or heavy lifting may also cause a disk to herniate.

This deterioration and bulging is common enough that doctors believe in itself it does not represent a health condition that requires treatment. However, the situation becomes problematic when the herniation places pressure against the roots of the SPINAL NERVES or the SPINAL CORD, causing PAIN and weakness or numbness in the leg (typically only one leg). Though symptoms may seem to start suddenly, they reflect processes that usually have been under way for a considerable time.

Symptoms and Diagnostic Path

The main symptom of herniated disk is sharp, shooting pain in the low back and in the leg (called radiculopathy). The pain in the leg is more significant for many people, and the leg may feel weak or numb in certain areas, depending on which spinal NERVE roots the herniation compresses. Some people experience discomfort in both legs, may have difficulty walking, and may have partial or complete loss of bladder or bowel function.

Sudden loss of bladder or bowel control is a serious symptom that requires immediate evaluation from a doctor.

The diagnostic path begins with a comprehensive medical examination, including NEUROLOGIC EXAMINATION and detailed PERSONAL HEALTH HISTORY. Diagnostic imaging procedures such as X-RAY of the spine, COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), and myelography (dye injected into the spinal column and viewed with X-ray) often reveal the location and severity of the herniation. The doctor may also request nerve conduction studies and electromyogram (EMG) to assess neuromuscular function. It is possible for diagnostic tests to be unable to pinpoint the precise cause of the symptoms, which does not necessarily rule out herniation.

Treatment Options and Outlook

Most doctors prefer, and most people respond to, conservative, nonsurgical treatment that targets relieving the pain and INFLAMMATION. Such an approach may include

- NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)
- heat or cold to the area

- limited activity for two to three days to allow the inflammation to subside
- MUSCLE RELAXANT MEDICATIONS to relieve MUSCLE SPASM
- structured, progressive PHYSICAL THERAPY including strengthening exercises for the back and proper techniques for lifting
- gradual return to regular activities

When pain is severe or does not respond to oral medications the doctor may inject the area with a corticosteroid medication in combination with a local anesthetic. Such an injection typically provides rapid and direct relief that lasts from several weeks to several months and may be sufficient to heal the damage to the disk.

A small percentage of disk herniations continue to cause pain and interfere with normal activities after conservative treatment efforts. In such situations, the doctor may recommend LAMINECTOMY, a surgical OPERATION to remove the damaged disk. Health experts strongly encourage a second opinion consultation with another doctor who specializes in treating back conditions before agreeing to back surgery. Though successful back surgery both relieves pain and restores function, complications are high enough to have earned designation as a health condition themselves: failed back surgery syndrome (FBSS). Both orthopedic surgeons and neurosurgeons perform surgeries for conditions of the spine; it is often valuable to have opinions from each type of doctor before making a decision about back surgery.

Risk Factors and Preventive Measures

The key risk factors for herniated nucleus pulposus are age and sudden stress to the back such as heavy lifting or traumatic injury. Cigarette smoking accelerates normal processes of deterioration and reduces the flow of BLOOD to the structures of the spine. Regular physical exercise to strengthen back muscles and abdominal muscles improves support for the spine, helping maintain proper alignment of the vertebrae to reduce wear and deterioration. Proper lifting methods reduce strain on the back. Though there are no measures to prevent herniation, such measures help protect the spine from injury that exacerbates other factors. Most people recover from an episode of ACUTE PAIN with conservative treatment and are able to return to their regular activities.

See also BACK PAIN; CHRONIC PAIN; SCIATICA; SMOKING CESSATION; SURGERY BENEFIT AND RISK ASSESSMENT.

hip fracture in older adults An injury, often preventable, that often results in significant disability or premature death. One in four hip fractures in adults over age 50 results in limited mobility after HEALING; one in four is fatal. Hip FRACTURE becomes a risk with increasing age for a combination of factors that include

- increasing loss of BONE and MUSCLE mass resulting in decreased STRENGTH and unsteady balance
- slowed reflexes and physical reactions
- diminished VISUAL ACUITY
- OSTEOPOROSIS (a condition of thin, weak bones due to loss of BONE DENSITY)
- health conditions such as ALZHEIMER'S DISEASE that impair judgment
- health conditions such as PARKINSON'S DISEASE that impair mobility
- medication side effects such as drowsiness, dizziness, and orthostatic HYPOTENSION (a sudden drop in BLOOD PRESSURE that occurs when rising)

Falls, two thirds of which occur in the home, account for 95 percent of hip fractures. Risks include loose rugs on the floor, uneven or slippery walking surfaces, and objects out of place that become obstacles. Though women are more likely to fracture a hip in a fall, men are more likely to die after hip fracture. Hip fracture has such a poor prognosis because recovery requires extended immobility, which has high risk for complications such as BLOOD clots and PNEUMONIA. Older adults are often reluctant to tell family members or their doctors when they fall for fear of losing independence. Efforts to reduce the risk for falls are the most effective measures for preventing hip fracture. Measures to strengthen bone and muscle, such as daily walking and light RESISTANCE EXERCISE (weightlifting), also help.

See also ACCIDENTAL INJURIES; QUALITY OF LIFE; REFLEX.

I–J

infectious arthritis INFLAMMATION of a JOINT that results from INFECTION. The infectious agent (PATHOGEN) may be BACTERIA or mycobacteria or a VIRUS, or fungus and travels to the joint through the BLOOD circulation. Infectious arthritis, also called septic arthritis, may also develop as a consequence of contamination during surgery on the joint. The doctor may withdraw fluid from the infected joint to examine its cells and determine the causative pathogen.

Immediate treatment with the appropriate ANTIBIOTIC MEDICATIONS or ANTIFUNGAL MEDICATIONS is essential to limit damage to the joint. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) are effective for relieving inflammation, PAIN, and FEVER associated with infectious arthritis. Sometimes needle aspiration or surgery is necessary to drain accumulated pus from the joint. With prompt and appropriate treatment, most people recover from infectious arthritis with few or no complications or long-lasting residual effects.

See also OSTEOARTHRITIS; RHEUMATOID ARTHRITIS; SYNOVITIS; TENDONITIS.

joint An articulating structure that connects two or more BONE surfaces to allow movement. The movement may be slight or the joint fused, such as the sutures in the cranium (skull). A joint may function like a hinge, such as the knee and elbow, or like a ball and socket, such as the hip and shoulder. In the carpal (hand) and tarsal (foot) joints, the bones glide along each other. Synovial capsules enclose joints that allow extensive movement between the bone surfaces, such as the knees, hips, and shoulders. The synovial membrane produces synovial fluid, which lubricates the bone ends within the joint to reduce friction between or among the structures of the joint during movement. Joints are particularly vulnerable to injury and damage resulting from repetitious motion.

HEALTH CONDITIONS INVOLVING THE JOINTS

ADHESIVE CAPSULITIS	ANKLE INJURIES
ANKYLOSING SPONDYLITIS	ARTHROGRYPOSIS
CONGENITAL HIP DYSPLASIA	CONTRACTURE
DISLOCATIONS	EPICONDYLITIS
INFECTIOUS ARTHRITIS	KNEE INJURIES
NEUROGENIC ARTHROPATHY	OSTEOARTHRITIS
RHEUMATOID ARTHRITIS	SYNOVITIS

For further discussion of joints within the context of the structures and functions of the musculoskeletal system, please see the overview section "The Musculoskeletal System."

See also BURSA; JOINT REPLACEMENT; LIGAMENT; MUSCLE; OSTEOARTHRITIS; TENDON.

joint replacement A surgical OPERATION, also called total JOINT replacement, to remove a severely diseased or damaged joint and replace it with a prosthetic joint. OSTEOARTHRITIS and RHEUMATOID ARTHRITIS are often to blame for joint deterioration severe enough to require joint replacement. The most commonly replaced joints are hips, knees, and shoulders. Prosthetic joints are also available for fingers, elbows, and ankles. Prosthetic joints are made of a variety of materials, usually combinations of metals (such as titanium) and plastic composites (such as polyethylene) that are durable, strong, and light.

Surgical Procedure

Joint replacement requires a hospital stay of three to seven days. The surgeon performs the operation with the person under general ANESTHESIA. For hip or knee replacement, an option is epidural or

spinal anesthesia with sedation for comfort. A joint replacement operation takes about two hours, during which the surgeon makes an incision large enough to adequately expose the joint, cuts away the damaged joint structures, prepares the remaining BONE structure to receive the prosthesis, and cements or otherwise attaches the prosthesis components into place. After the surgeon finishes the operation, the person goes to the recovery unit for close nursing supervision and care until the anesthesia wears off and PAIN control is satisfactory, usually for two to four hours.

Return to activity begins almost immediately and is essential for full recovery of joint function. It is especially important for the person to begin walking right away for hip and knee replacements. The doctor will prescribe ANALGESIC MEDICATIONS for pain relief. Intensive PHYSICAL THERAPY moves the new joint through passive and active range of motion exercises. Frequent walking also reduces the risk for blood clots. The doctor may prescribe medication, support stockings, or inflatable compression cuffs.

Risks and Complications

All surgeries carry the risk for excessive bleeding during or after the operation, blood clots, and INFECTION of the surgical wound. A particular risk with joint replacement is infection that infiltrates the bone, causing more extensive damage than a repeat joint replacement could repair. Other potential complications of joint replacement include failure of the prosthesis, loosening of the insertion of the prosthesis into the bone ends, DISLOCATIONS, and loss of function due to wear over time.

Outlook and Lifestyle Modifications

A prosthetic joint has a life expectancy of 5 to 15 years, depending on the joint and the person's lifestyle. Some strenuous physical activities may no longer be possible, depending on the replaced joint. A replacement hip or knee generally cannot tolerate activities such as running and jumping, for example, though swimming and bicycling are excellent alternatives for aerobic conditioning and improving STRENGTH, ENDURANCE, and FLEXIBILITY. Most people who undergo joint replacement enjoy vastly improved QUALITY OF LIFE after HEALING is complete. Complete rehabilitation and return to normal activities may take three to six months.

See also PATIENT CONTROLLED ANALGESIA; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; PROSTHETIC LIMB; SURGERY BENEFIT AND RISK ASSESSMENT.

K

knee injuries Sprains, strains, CARTILAGE tears, and fractures involving the structures of the knee. The knee is a hinge JOINT that allows the leg to flex (bend back) and straighten, essential actions of walking. Unique among hinge joints in the body, the knee also allows a small amount of rotation. The knee is vulnerable to both traumatic and repetition injuries. Knee injury is the leading reason for visits to orthopedic surgeons in the United States.

The knee primarily joins the femur (thigh BONE) to the tibia (shin bone) and the fibula (small long bone behind the tibia). It also contains the patella (kneecap), a small bone that provides added leverage for movement of the lower leg. A C-shaped thick pad of cartilage, the meniscus, cushions the ends of the bones from each other. Each knee contains two menisci: the medial meniscus, which wraps around the inside of tibia, and the lateral meniscus, which wraps around the outside of the tibia. Strong ligaments bind the knee from each side and the center, holding the bones in place.

The most damaging traumatic injuries to the knee are those that result from a blow or fall that rapidly stretches the ligaments and causes them to tear (ligament sprain). Sudden twisting motions in which the foot plants but the rest of the leg continues to move also expose the knee to such injury. The knee takes considerable pounding in the course of everyday activities that subject it to repeated impact (such as occurs with walking, running, and jumping). Repetition or "wear and tear" injuries of the knee include OSTEOARTHRITIS and PATELLOFEMORAL SYNDROME.

Symptoms and Diagnostic Path

PAIN and swelling are symptoms common to many kinds of knee injuries. Damage to ligaments and menisci often result in an unstable knee that feels "loose" or may not bear the person's weight. With a moderate to severe injury the person hears and feels a substantial "pop" from the knee, which is the LIGAMENT tearing. Depending on which ligament the injury damages, the knee may feel it wants to bend too far back, extend too far forward, or slip to one side or the other. A significant blow to the side of the knee can cause multiple injuries within the knee, rendering the knee useless. Hyperextension and dislocated patella present characteristic appearances that make the diagnosis obvious. A fractured patella can cause excruciating pain and complete inability to use the knee or leg.

The diagnostic path begins with a detailed accounting of the nature of the pain and description of any precipitating trauma. The doctor will thoroughly examine both knees. Diagnostic procedures may include X-RAY, especially if the doctor suspects a FRACTURE, though COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) typically yield more information about the nature and extent of soft tissue injuries such as are most common in the knee. Diagnostic ARTHROSCOPY, a MINIMALLY INVASIVE SURGERY, may be necessary to fully assess the damage and has the advantage of allowing the surgeon to immediately repair the injury.

Treatment Options and Outlook

Ice to the knee and restricting movement are the most effective immediate treatments for traumatic injury. Prompt icing can reduce INFLAMMATION and swelling to minimize the severity of the injury. Suspected patella fracture or severe sprain requires immobilization to prevent further damage. Many knee injuries heal with conservative, nonsurgical treatment approaches. The doctor may recommend a knee wrap or brace, depending on the injury. NONSTEROIDAL ANTI-INFLAMMATORY

COMMON KNEE INJURIES

Injury	Common Causes	Key Symptoms
anterior cruciate LIGAMENT (ACL) sprain	sudden twisting of the knee or blow to the front of the knee	pop or snap felt and heard swelling mild PAIN "loose" feeling to knee inability to bear weight on the leg
hyperextension	direct blow to the front of the knee	pain with hyperextension soreness after knee returns to normal extension
lateral collateral ligament (LCL) sprain	impact to the inside of the knee	pain pop or snap felt and heard knee buckles to the outside
medial collateral ligament (MCL) sprain	impact to the outside of the knee	pain pop or snap felt and heard knee buckles to the inside
meniscus tear	sudden rotation of the upper body with the foot planted	pain clicking or locking within the knee instability of the knee
patella DISLOCATION	impact to the side of the patella fall that jars the side of the patella	pain patella obviously out of position, usually to the side of the knee inability to bend the knee
patella FRACTURE	sharp blow to the patella	severe pain and swelling inability to move the knee or bear weight on the leg
patellar TENDON rupture	stumbling in an attempt to avoid a fall landing after a jump from considerable height	pain tenderness to touch at point of rupture difficulty bending or extending the lower leg displaced patella
PATELLOFEMORAL SYNDROME	long-term repetitious movement of the knees such as with running and bicycling poor conditioning	pain with bending or extending the knee
posterior cruciate ligament (PCL) sprain	impact or blow to the front of the knee	pop or snap felt and heard swelling mild pain "loose" feeling to knee inability to bear weight on the leg

STAGE SCALE: LIGAMENT SPRAIN OR TEAR

Grade	Extent of Injury or Damage	Symptoms
grade 1 or first degree	minor stretching of LIGAMENT fibers though knee remains stable	mild PAIN with pressure to the knee mild swelling
grade 2 or second degree	moderate tear of the ligament with some instability of the knee	moderate pain with pressure to the knee moderate swelling
grade 3 or third degree	complete tear of the ligament and its nerves; unstable knee	little if any pain with pressure to the knee pronounced pop felt and heard at time of injury inability to bear weight or use the knee

DRUGS (NSAIDS) relieve inflammation and pain for both traumatic and overuse injuries. Gentle stretching and exercise such as walking help keep the knee flexible and facilitate HEALING.

Mild to moderate ligament sprains often heal without surgery in four to six weeks. Severe ligament sprains and meniscal tears often require surgery to repair. Orthopedic surgeons can perform nearly all such operations arthroscopically, which allows minimal recovery time. PHYSICAL THERAPY facilitates rehabilitation after surgery and most people able to return to regular activities in about six months. Return to sports may require more time, especially for activities of high vulnerability for knee injury such as football, soccer, downhill skiing, and basketball.

Risk Factors and Preventive Measures

Contact sports (such as football) and other sports that involve running, twisting, and jumping (such as soccer, basketball, and tennis) expose the knee to direct blows with great risk for injury. Any sport that uses cleats to improve traction (such as track, soccer, and football) has increased risk for knee injury resulting from excessive torsion (twisting under pressure). Sports and athletic activities account for the majority of knee injuries in people under age 25. By midlife, repetitive trauma (such as results from running) begins to take its toll and overuse injuries become more common. Excessive body weight further stresses the knees.

Strong thigh muscles—the quadriceps in the front and the hamstrings in the back—improve stability of the knee. Weight-lifting or RESISTANCE EXERCISE can strengthen these muscles. YOGA is excellent for improving FLEXIBILITY as well as stability of the knees. Knee supports, braces, and protective pads reduce the risk of knee injury in some sports. Proper technique and adequate physical conditioning are crucial elements of injury prevention for any athletic activity. Other preventive measures include stretching and WARM-UP before and after participating in vigorous exercise or sports events.

See also ANKLE INJURIES; ATHLETIC INJURIES; OSGOOD-SCHLATTER DISEASE; STRENGTH; WALKING FOR FITNESS.

kyphosis A deformity of the upper spine that gives the appearance of a hump in the upper back. Kyphosis may represent a CONGENITAL ANOMALY in the structure of the spine or may develop later in life as a consequence of damage to the CARTILAGE disks between the vertebrae that allow the vertebrae to slide out of position. Mild kyphosis generally does not cause symptoms and may be noticeable only with X-rays of the spine. Moderate kyphosis can cause upper BACK PAIN, resulting from distorted posture that strains the back muscles. Treatment may include PHYSICAL THERAPY or CHIROPRACTIC care to stretch the back, strengthen muscles, and improve posture. Sometimes sleeping on a very firm mattress with a low pillow allows the spine to correct itself. The doctor may prescribe a back brace for moderate kyphosis. Severe kyphosis may require surgery to realign and support the vertebrae.

See also ACHONDROPLASIA; LORDOSIS; OSTEOPOROSIS; SCOLIOSIS; X-RAY.

L

laminectomy A surgical OPERATION to remove a segment of vertebra (BONE of the spine) to relieve pressure against the SPINAL CORD or a spinal NERVE root. Laminectomy treats neurologic symptoms arising from HERNIATED NUCLEUS PULPOSUS (herniated or slipped disk), CERVICAL SPONDYLOSIS, and SPINAL STENOSIS. When laminectomy is the appropriate therapeutic choice, it has a fairly high success rate for relieving symptoms (such as PAIN, weakness, and numbness in the leg) and allowing the person to return to regular activities. However, it is important to first consider all other therapeutic options as the rate of success for back surgery is highly variable.

Laminectomy is an OPEN SURGERY on the back performed under general ANESTHESIA. An orthopedic surgeon or a neurosurgeon may perform the operation. The surgeon makes a long incision (five to seven inches) along the spine at the site of the impingement; separates the soft tissue structures from the vertebra to expose the bone; and removes a lamina, one of the flat segments of the vertebral arch. Depending on the cause of the impingement and the overall health of the vertebrae (whether there is progressive deterioration such as is common with spinal stenosis), the surgeon may choose also to fuse the operated vertebra to an adjacent healthy vertebra for stability. Most people stay in the hospital up to three days after the operation. Recuperation and return to normal activities takes six to eight weeks.

The risks of laminectomy include excessive bleeding during surgery, postoperative INFECTION, continued symptoms after HEALING, and sensory disturbances resulting from surgical injury to the spinal nerve root. When the cause of the nerve compression was deterioration of the vertebra due to a progressive condition such as OSTEOARTHRITIS, further damage may occur to the same vertebra or other vertebrae. About 70 percent of people experience full relief from their symptoms and return to work and recreational activities without restriction.

See also BACK PAIN; SCIATICA; SPINAL NERVES; SURGERY BENEFIT AND RISK ASSESSMENT.

ligament A cordlike structure of tough connective tissue that binds bones together at joints. Ligaments are vulnerable to injury from stretching, which can cause them to tear. Such a ligament injury is a sprain. Most sprains heal with conservative treatment, though some (notably complete tears) require surgery to repair them. Ligaments may also join or support organs and structures other than bone, such as the round ligaments in the pelvis that suspend the UTERUS within the abdominal cavity.

See also BONE; JOINT; MUSCLE; SPRAINS AND STRAINS; TENDON.

lipoma A benign (noncancerous) soft tissue tumor. Lipoma is the most common type of tumor. It arises from adipocytes—fat cells—though can develop in any kind of tissue. Lipomas are particularly common in the MUSCLE, appearing as a small painless lump. A lipoma near the surface of the SKIN feels soft and fairly well defined. Lipoma does not hurt or become cancerous and requires no treatment unless it becomes larger than five centimeters. Large lipomas may be cosmetically unacceptable or cause irritation to the surrounding tissue. The doctor may choose to biopsy or remove a lipoma that occurs in the BREAST or COLON, to be certain of the diagnosis as other kinds of breast and colon tumors may be malignant (cancerous). Lipomas have a tendency to recur after surgery to remove them.

See also ADENOMA; BREAST CANCER; COLORECTAL CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

lordosis An abnormally exaggerated inward curvature of the lumbar spine at the small of the back, giving the appearance of protruding buttocks in the back and protruding belly in the front. Lordosis may result from congenital abnormalities of the spine and often develops when a child begins to walk. CONGENITAL HIP DYSPLASIA, CEREBRAL PALSY, SPINA BIFIDA, and neuromuscular disorders in which the muscles are weak are common congenital causes for lordosis. Lordosis is also common in ACHONDROPLASIA and other forms of SKELETAL DYSPLASIA.

Lordosis does not usually cause symptoms other than its appearance. Sometimes lordosis results from habitual poor posture. X-RAY is usually sufficient to confirm the diagnosis. Treatment attempts to prevent progression of the curvature as well as to correct the existing deformity to retain spinal stability for support of the axial SKELETON. However, most lordosis in otherwise healthy children corrects itself as the child grows.

See also CONGENITAL ANOMALY; KYPHOSIS; SCOLIOSIS; SURGERY BENEFIT AND RISK ASSESSMENT.

Marfan syndrome A genetic disorder arising from mutations in the *fbn1* GENE that affect the structure of connective tissues throughout the body. The *fbn1* gene encodes for fibrillin 1, a protein molecule essential for the formation of elastin. Elastin is the basis of the fibers that form the connective tissues. In Marfan syndrome the elastin is too soft, allowing connective tissues to stretch more than normal. The INHERITANCE PATTERN for Marfan syndrome is autosomal dominant, meaning one parent who has the mutated gene can pass the condition to his or her children. Marfan syndrome primarily affects the cardiovascular system, musculoskeletal system, and eyes.

Symptoms and Diagnostic Path

Marfan syndrome produces hallmark physical characteristics that include

- tall, lanky frame with extraordinarily long arms
- elongated, narrow face
- crowded TEETH
- narrow, sunken chest
- long, thin fingers

Many people who have Marfan syndrome have severe MYOPIA (nearsightedness) and abnormalities of the CORNEA. Within the body, one of the most significant effects of Marfan syndrome is on the major BLOOD vessels, notably the AORTA, and the HEART valves. Because the connective tissue within the walls of the arteries is softer than it should be, the walls of the arteries are susceptible to separation (ANEURYSM). As well, the heart valves are often larger than normal and do not close properly, allowing blood to backflow within the heart. Mitral valve prolapse is the most common manifestation of this aspect of Marfan syndrome. To compensate, the heart intensifies the STRENGTH and frequency of its contractions, which over time enlarges the heart (CARDIOMYOPATHY).

There are no definitive diagnostic tests for Marfan syndrome, and symptoms are sometimes mild enough to escape detection until midlife or later when cardiovascular problems begin to emerge. An accumulation of symptoms points to the diagnosis, particularly if there is a family history of Marfan syndrome. The doctor may conduct GENETIC TESTING for the *fbn1* gene MUTATION to confirm the diagnosis.

Treatment Options and Outlook

Treatment focuses on early detection of and therapy for potential complications, notably CARDIOVASCULAR DISEASE (CVD). Doctors advise against activities, especially competitive sports, that cause rapid and extreme changes in BLOOD PRESSURE and HEART RATE. Treatment may include medications to maintain low blood pressure and heart rate as preventive measures. Most people who have Marfan syndrome should have an ECHOCARDIOGRAM (ULTRASOUND examination of the heart) annually to screen for changes in the heart's size and valve function and the stability of the aorta. Early surgery to intervene when echocardiogram suggests a dissecting aortal aneurysm can be lifesaving.

Risk Factors and Preventive Measures

Because cardiovascular complications of Marfan syndrome can be severe or life threatening, doctors recommend GENETIC COUNSELING for people who have the disease. Marfan disease is preventable only by preventing transmission of the mutated *bfn1* gene. For the 30 percent or so of people in whom the mutation is spontaneous

(occurs without apparent family history of the condition), there are no measures of prevention.

See also GENETIC DISORDERS.

meniscectomy A surgical OPERATION to remove part or all of a damaged meniscus in the knee. Each knee has two menisci, C-shaped pads of CARTILAGE that cushion the ends of the femur (thigh BONE) and tibia (shin bone) as they come together within the knee JOINT. Meniscus tears are common ATHLETIC INJURIES and occur when there is torsion under pressure—the body above the knee twists suddenly during movement but the foot remains planted. Most of the time the orthopedic surgeon can perform a partial meniscectomy with ARTHROSCOPY (MINIMALLY INVASIVE SURGERY using a specialized endoscope), which allows rapid recovery and return to regular activities.

Cartilage, which is very dense, does not have its own BLOOD supply but rather draws necessary NUTRIENTS from surrounding tissues and fluids. Tears near the outer edge of the meniscus are more likely to heal than tears in the center of the meniscus. The surgeon may attempt to repair an outer tear though will likely need to remove the damaged segments of meniscus when the tear is interior. The goal is to remove as little of the meniscus as possible because without it the bone ends loose protection. It is equally important to remove any pieces of the meniscus that are torn or fragmented to prevent them from "jamming" the joint.

The risks of meniscectomy include excessive bleeding during surgery and postoperative INFECTION, both of which are rare. Full recovery after arthroscopic surgery takes about six weeks and after OPEN SURGERY may take up to six months. Even after HEALING, complete meniscectomy may limit some athletic activities that place significant stress on the knee, such as downhill skiing.

See also KNEE INJURIES; PHYSICAL THERAPY; SURGERY BENEFIT AND RISK ASSESSMENT.

muscle Contractile fibers or the structures these fibers form. Muscles move the body, some under voluntary control and others reflexively. The gastrointestinal tract, genitourinary tract, and BLOOD vessels contain smooth (nonstriated) muscle, which is under involuntary control of the autonomic NERVOUS SYSTEM. The HEART contains a specialized form of muscle called myocardial, also under control of the autonomic nervous system. The bulk of the muscle tissue in the body is skeletal (striated) muscle, which responds to voluntary control through the CENTRAL NERVOUS SYSTEM.

The skeletal muscles are responsible for movement and account for about 40 percent of the body's mass. They generally appear in opposing pairs attached to BONE via tendons. When one muscle contracts, its opposing muscle relaxes. This allows smooth, balanced movement. The SKELETON provides resistance and leverage for the muscles as they contract and relax. The body contains about 650 muscles, the largest of which is the gluteus maximus (main muscle of the buttocks) and the smallest of which is the stapedius in the middle EAR (moves the stapes bone).

Movement requires interaction between neurons (NERVE cells) and muscle fibers. This interaction occurs at the neuromuscular junction, a synapse where the NEURON's axons end (terminate) and the muscle fiber begins. When conveying a nerve impulse to activate a skeletal muscle fiber, the motor neuron releases a molecule of acetylcholine, a NEUROTRANSMITTER. The acetylcholine molecule binds with an acetylcholine receptor on the muscle fiber, forming a biochemical bridge that allows the nerve impulse to travel from the neuron to the muscle fiber. The impulse creates an action potential in the muscle fiber—a cycle of activation, discharge, and recovery—that becomes a muscle contraction.

Skeletal muscles contain two types of fiber that dictate how rapidly and with what intensity they complete an action potential. Type 1 fibers, also called slow-twitch or red fibers (red because they have a high myoglobin content), have a slow and steady response. Type 1 fibers are in a constant state of partial contraction; they provide muscle tone and are essential for maintaining the body's posture. Type 2 fibers, also called fast-twitch or white fibers (white because they contain very little myoglobin), have a rapid response. Type 2 fibers are responsible for muscle STRENGTH. Most skeletal muscles contain a combination of type 1 and type 2 fibers. Exercise to extend ENDURANCE increases the percentage of type 1 fibers; exercise to improve strength increases the percentage of type 2 fibers.

For further discussion of muscle within the context of the structures and functions of the musculoskeletal system, please see the overview section "The Musculoskeletal System."

See also CELL STRUCTURE AND FUNCTION; FASCIA; LIGAMENT; PROPRIOCEPTION; TENDON.

muscle relaxant medications Medications that relieve MUSCLE spasms, cramps, and stiffness. Some muscle relaxants are also called antispasmodic medications. Doctors may prescribe these medications to treat acute BACK PAIN, acute sprains, severe muscle tension HEADACHE, and muscle spasticity due to conditions such as CEREBRAL PALSY, MULTIPLE SCLEROSIS, SPINAL CORD INJURY, MUSCULAR DYSTROPHY, FIBROMYALGIA, and many others. There are various types of muscle relaxant medications that work through different mechanisms, though all act on the CENTRAL NERVOUS SYSTEM rather than on the muscles directly. Because of this, most muscle relaxants also affect alertness, balance, and other neurologic functions.

As with any medication, muscle relaxants can have adverse side effects and interact with other drugs, including OVER-THE-COUNTER (OTC) DRUGS and herbal remedies. Typically muscle relaxants provide short-term relief during acute injury. Once muscle fibers begin to heal, they return to normal contraction and relaxation patterns and muscle relaxant medications are no longer necessary or helpful for recovery. Muscle relaxants in the benzodiazepine family of drugs (such as diazepam) cause significant drowsiness and can become habit forming; doctors generally prescribe them sparingly because of these risks.

COMMON MUSCLE RELAXANT MEDICATIONS

carisoprodol	chlorzoxazone
cyclobenzaprine	diazepam
metaxalone	methocarbamol

See also ADVERSE REACTION; CRAMP; DRUG INTERACTION; MEDICINAL HERBS AND BOTANICALS; PHYSICAL THERAPY; SPRAINS AND STRAINS; SPASM.

muscular dystrophy The collective term for a group of GENETIC DISORDERS of the MUSCLE resulting in progressive weakness. Most types of muscular dystrophy arise from a deficiency of the protein dystrophin, which is essential for skeletal (striated) muscle cell integrity and function. Without it the skeletal muscles deteriorate and movement becomes difficult or impossible. About 50,000 Americans have muscular dystrophy. The three most common of the nine major types of muscular dystrophy are Duchenne's muscular dystrophy, facioscapulohumeral muscular dystrophy, and myotonic muscular dystrophy.

Duchenne's muscular dystrophy Duchenne's is an X-linked recessive MUTATION affecting the dystrophin GENE. As such, it nearly exclusively affects boys. Symptoms begin to appear in early childhood with characteristic postures and gait. Progression is steady, and most boys who have Duchenne's lose the ability to walk by about age 12. The skeletal muscles of the upper chest become involved in ADOLESCENCE, affecting BREATHING. Duchenne's is usually fatal before age 20.

A milder presentation of similar symptoms and pattern of progression with a later age of onset (late childhood or early adolescence) is Becker's muscular dystrophy. Though the course of the disease is ultimately fatal, most who have it live into their 30s. Treatment is primarily supportive, with PHYSICAL THERAPY to help preserve muscle STRENGTH and function. CORTICOSTEROID MEDICATIONS may improve symptoms.

Facioscapulohumeral muscular dystrophy An adult-onset type of muscular dystrophy, facioscapulohumeral muscular dystrophy affects men and women equally. Symptoms first appear as weakness in the muscles of the face and shoulder girdle (upper arms and shoulders). The shoulders often "wing" outward. Over the course of the disease, muscle weakness moves downward through the body though the lower arms are usually the last affected. Symptoms are mild enough in about half of those who have this form of muscular dystrophy to permit fairly normal function and mobility throughout life. In others, symptoms may affect swallowing and mobility.

Myotonic muscular dystrophy In myotonic muscular dystrophy the muscles lose the ability to relax after contraction, causing them to become stiff. Myotonic muscular dystrophy is the most common type of adult-onset muscular dystrophy and affects men and women equally. The cause is a mutation in the gene that encodes for myotonica protein

MAJOR TYPES OF MUSCULAR DYSTROPHY

Type of Muscular Dystrophy	Key Characteristics	Inheritance Pattern
Duchenne's	most common type affects primarily muscles of the upper arms, upper legs, and pelvic girdle first symptoms usually appear between ages 2 and 6	X-linked recessive
myotonic	affects primarily muscles of the face and neck, hands, and feet gastrointestinal, cardiac, EYE, neurologic, and endocrine involvement later in the disease first symptoms appear in adulthood	autosomal dominant
Becker's	affects primarily muscles of the upper arms, upper legs, and pelvic girdle very similar to Duchenne's with milder symptoms symptoms begin in late childhood or early ADOLESCENCE	X-linked recessive
limb-girdle	affects primarily the muscles of the pelvic girdle and shoulder girdle symptoms begin in late adolescence or early adulthood	autosomal recessive or autosomal dominant
facioscapulohumeral	affects primarily the muscles of the face, neck, and shoulders symptoms begin in late adolescence or early adulthood	autosomal dominant
congenital	affects all skeletal muscles often affects the CENTRAL NERVOUS SYSTEM, causing seizures symptoms are present at birth	autosomal recessive
oculopharyngeal	affects the muscles of the eyelids and THROAT symptoms begin in middle to late adulthood	autosomal dominant
distal	affects the forearms, hands, lower legs, and feet symptoms begin in adulthood	autosomal recessive or autosomal dominant
Emery-Dreifuss	affects primarily the shoulders, upper arms, pelvis, and lower legs symptoms typically appear first as contractures, then weakness symptoms begin in late childhood or early adolescence	X-linked recessive

kinase. Other gene mutations may also contribute. Though progression is usually slow, myotonic muscular dystrophy affects other body systems as well. Cataracts and diabetes are common.

Symptoms and Diagnostic Path

In most forms of muscular dystrophy, the primary symptoms are muscle weakness and disturbances of posture and gait (walking style). The diagnostic path begins with detailed PERSONAL HEALTH HISTORY and family health history. Because muscular dystrophies are inherited disorders, the family health history is particularly important. A comprehensive NEUROLOGIC EXAMINATION identifies the specific symptoms, which helps narrow the diagnosis. BLOOD tests may show excessive proteins that indi-

cate muscle destruction. Each type of muscular dystrophy has fairly characteristic patterns of symptoms. Muscle biopsy shows damage to the muscle cells.

Treatment Options and Outlook

Treatment for all types of muscular dystrophy is primarily supportive. Physical therapy, braces, orthotics, and mobility aids extend the ability to walk and function independently. Corticosteroid medications slow the progression of symptoms in some types of muscular dystrophy, notably Duchenne's. Though all types of muscular dystrophy are lifelong, muscular dystrophy is not necessarily fatal. Many people with milder types of the disease live normal life expectancy with relative independence.

Risk Factors and Preventive Measures

Muscular dystrophy is always inherited, so the key risk factor is family history. People who have muscular dystrophy or family history of muscular dystrophy should consider GENETIC COUNSELING to aid in FAMILY PLANNING decisions. There are no measures known to prevent muscular dystrophy, though research holds hope for GENE THERAPY that can someday correct the mutations that cause the disease.

See also CATARACT; MYOPATHY.

myasthenia gravis A rare autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that target acetylcholine receptors on the cell membrane surfaces of MUSCLE cells. Acetylcholine is a NEUROTRANSMITTER that carries NERVE impulses from neurons to muscle cells to initiate movement. Acetylcholine receptors are specialized molecules that bind acetylcholine molecules, a process analogous to plugging an electrical cord into an outlet. The NEURON releases acetylcholine to carry the impulse across the synapsis to the muscle cell. Binding forms a complete circuit and the nerve impulse passes from the neuron to the muscle cell.

The antibodies present in myasthenia gravis attack and destroy acetylcholine receptors, reducing the ability of acetylcholine to carry to completion the nerve impulses that direct movement. Because there are fewer acetylcholine receptors in myasthenia gravis, the acetylcholine molecule the neuron releases often dissipates before a receptor becomes available. As a result, muscle contractions are weak. Muscles that have the fewest numbers of acetylcholine receptors to begin with—the muscles of the eyelids, eyes, face, MOUTH, and THROAT—are the most dramatically affected. Muscle function worsens during activity that uses affected muscles, such as chewing or talking, and improves after rest.

Myasthenia gravis may develop at any age though is most common in women under age 40 and men over age 60. Researchers do not know what causes myasthenia gravis but suspect a dysfunction of the THYMUS, a structure of the immune system responsible for the maturation of T-cell lymphocytes, may play a significant role. The thymus, which normally has little function in adults, is abnormally active in people who have myasthenia gravis. Symptoms of myasthenia gravis relate to the muscles affected and may include difficulty focusing the eyes, slurred speech, or difficulty swallowing. Involvement of peripheral muscles may result in balance and gait dysfunctions.

Because myasthenia gravis is relatively rare, doctors typically explore more common causes for weak muscles before looking specifically for myasthenia gravis. BLOOD tests can detect the presence of the acetylcholine receptor antibodies in most people who have myasthenia gravis. Other diagnostic procedures that point to the disorder include specialized electromyogram (EMG) and tests that measure the muscle's response to acetylcholine.

Treatment includes anticholinesterase medications, which block the action of cholinesterase, an enzyme that breaks down acetylcholine, and IMMUNOSUPPRESSIVE MEDICATIONS, which interfere with the release of antibodies to slow the destruction of acetylcholine receptors. Many people experience significant improvement in their symptoms after THYMECTOMY (a surgical OPERATION to remove the thymus). Most people who have myasthenia gravis are able to enjoy relatively normal lives with appropriate treatment.

See also ANTIBODY; AUTOIMMUNE DISORDERS; IMMUNE RESPONSE; LYMPHOCYTE; SURGERY BENEFIT AND RISK ASSESSMENT; T-CELL LYMPHOCYTE.

myopathy MUSCLE weakness that occurs when muscle cells do not function properly. There are

numerous forms of myopathy, many of which are congenital (present at birth) or genetic (the result of inherited GENE mutations). Some myopathies are progressive (become worse with time) and others remain stable. Metabolic disorders, HIV/AIDS, IMMUNE DISORDERS, and ADVERSE REACTION to drugs (including ALCOHOL) may cause myopathies. Treatment targets the cause of the myopathy in acquired myopathy and attempts to relieve symptoms when myopathy is congenital or genetic. Treatment approaches may include medications, PHYSICAL THERAPY, braces or other devices to support weak muscle structures and aid mobility, and MASSAGE THERAPY.

See also CARDIOMYOPATHY; GENETIC DISORDERS; INHERITANCE PATTERN; MITOCHONDRIAL DISORDERS; MUTATION; NEUROPATHY; POLYMYOSITIS.

myotonia A neuromuscular circumstance in which the muscles contract properly but do not relax, causing temporary stiffness. Movement may be slow and difficult until the muscles warm up, after which they seem to function more smoothly. Myotonia may be a symptom, such as with some forms of MUSCULAR DYSTROPHY, or a congenital condition. Myotonia congenita is a rare form of myotonia that occurs as a result of GENE mutations. Some forms of myotonia are progressive though most are not. Myotonia is a disorder of the ion channels in the MUSCLE cells (channelopathy), most often the chloride, sodium, or potassium channels. The ion channels regulate the ion exchange that must occur for a cell to "fire," which in the case of muscle cells is to contract and relax.

The diagnosis of myotonia is primarily clinical, based on the doctor's observance of the person's movement and muscle function. Characteristic alterations in the electromyogram (EMG) generally can confirm the diagnosis. Treatment with antiseizure medications and drugs that affect the ion channels often improve symptoms and muscle function. Myotonia resulting from another disorder often improves when the underlying condition improves. Though myotonia is a lifelong circumstance, most people who have myotonia are able to enjoy fairly normal lifestyles with appropriate medication therapy.

See also CELL STRUCTURE AND FUNCTION; GENETIC DISORDERS; INHERITANCE PATTERN; MUTATION; MYOPATHY; NEURON.

neurogenic arthropathy Degeneration of a JOINT, commonly the knee, as a consequence of NEUROPATHY (impaired NERVE function) that causes loss of sensation. Injuries occur to the affected joint because there is limited perception of PAIN or sense of the joint's position relative to the body and its immediate environment (PROPRIOCEPTION). Neurogenic arthropathy sometimes called Charcot's joints, often includes unrecognized fractures that do not heal properly because the joint is in continuous motion. As a result the joint becomes deformed and dysfunctional, changes that cause only mild discomfort because of the underlying NEUROPATHY.

The diagnostic path begins with recognition of the underlying neuropathy. X-RAY can usually confirm the damage to the joint. Treatment for neurogenic arthropathy aims to preserve joint structure and function to the extent possible and may include BONE graft or surgery to stabilize the joint. Some people are good candidates for JOINT REPLACEMENT, though in progressive forms of neurogenic arthropathy the joint may continue to deteriorate around the prosthesis.

CONDITIONS ASSOCIATED WITH NEUROGENIC ARTHROPATHY

AMYLOIDOSIS	CHARCOT-MARIE-TOOTH (CMT) DISEASE
DIABETES	Hansen's disease (leprosy)
SPINA BIFIDA	SPINAL CORD INJURY

See also CHARCOT-MARIE-TOOTH (CMT) DISEASE; FRACTURE; INFECTIOUS ARTHRITIS; OSTEOARTHRITIS; RHEUMATOID ARTHRITIS.

occupational therapy A therapeutic approach to teach people the skills they need for living as independently as possible with long-term injury or disability. Occupational therapy focuses on techniques and devices to make easier the activities and events of daily living, aiding with such circumstances as recovery after STROKE, developmental disability in children, and rehabilitation after serious injury or surgery. The doctor may also recommend occupational therapy for people who have neuromuscular disorders, MYOPATHY, NEUROPATHY, and CHRONIC PAIN syndromes. Occupational therapists also conduct home visits to recommend environmental adaptations to reduce the risk of falls as well as to accommodate factors such as wheelchair accessibility. In the United States occupational therapy services require a prescription from a doctor.

See also PHYSICAL THERAPY; QUALITY OF LIFE.

Osgood-Schlatter disease A disorder of the epiphysis (growth plate) of the tibia, the long BONE in the lower leg (shin bone) that typically develops in athletically active adolescents. ADOLESCENCE is the period during which growth of the long bones is very rapid. The patellar TENDON stretches across the head of the tibia to attach at the top of the tibial tubercle. Athletic activities that extensively use the quadriceps MUSCLE in the thigh, such as basketball, place considerable pressure on the tendon insertion point. In Osgood-Schlatter disease, sometimes called jumper's knee, tiny fragments of developing bone tissue pull away from the epiphysis and become embedded in the tendon. As these fragments, called avulsion fractures, mineralize they form a hard lump just below the patella (kneecap).

The main symptoms of Osgood-Schlatter disease, also called osteochondrosis, are a noticeable lump and PAIN in the area of the knee. Pain is often more intense when going up and down steps, running, and jumping. Osgood-Schlatter disease tends to affect girls at a younger age (10 to 12 years) than it affects boys (12 to 14 years). The doctor bases the diagnosis on the presentation of symptoms and the findings on X-RAY studies. The doctor may also conduct a bone scan when the X-ray findings are unclear. However, diagnosis is usually straightforward.

Osgood-Schlatter disease is self-limiting; it goes away when growth in the tibia ceases. Ice to the area and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve INFLAMMATION and pain are generally sufficient treatment. A physical therapist or sports medicine specialist can teach the child stretching exercises for the quadriceps and for the hamstrings, in the back of the thigh, to reduce pressure against the patellar tendon.

See also ATHLETIC INJURIES; PHYSICAL THERAPY.

osteoarthritis A condition of progressive degeneration of the joints. Osteoarthritis tends to develop in adults age 60 and older and to affect joints subject to excessive stress throughout life, often in occupational settings. Recreational and athletic activities may also result in osteoarthritis. The fingers, cervical spine (neck), knees, hips, and lumbar spine (low back) are most commonly affected. About 20 million Americans have osteoarthritis.

Osteoarthritis damages CARTILAGE, the thin layer of smooth connective tissue that coats the ends of bones with the joints. Cartilage is so dense that it does not have its own BLOOD supply. Instead, it relies on adjacent tissues and the synovial fluid to supply it with the NUTRIENTS it requires. Cartilage cannot regenerate or rebuild itself so damage to it

is permanent. Osteoarthritis is a leading cause of disability in the United States.

Symptoms and Diagnostic Path

Many people who have osteoarthritis sufficient to show up on X-RAY have few if any symptoms. Researchers estimate that by age 60, more than half of Americans have radiologic evidence of osteoarthritis. However, fewer than 20 percent of Americans seek medical treatment for symptoms of osteoarthritis. Stiffness and PAIN in the joints are the main symptoms of osteoarthritis. Discomfort is usually greatest in the morning when first getting out of bed and after physical activity.

The diagnostic path may include X-ray to assess the extend of damage within painful joints. But because the damage primarily affects cartilage, a soft tissue, the full extent of osteoarthritis is not likely to be apparent with X-ray. The doctor may request other diagnostic procedures to rule out conditions that have similar symptoms. However, a detailed PERSONAL HEALTH HISTORY in combination with a comprehensive medical examination is generally sufficient for the doctor to make the diagnosis.

Treatment Options and Outlook

Treatment for osteoarthritis attempts to slow the degeneration by reducing INFLAMMATION. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and injections of CORTICOSTEROID MEDICATIONS are very effective in accomplishing this goal. NSAIDs also relieve pain. Other treatment includes easing the stress on the joints, daily physical exercise for WEIGHT LOSS AND WEIGHT MANAGEMENT, and measures such as moist heat to affected joints. Exercises can strengthen the muscles and other structures of the joints. YOGA is excellent for improving range of motion and FLEXIBILITY.

Though there are no treatments that can cure osteoarthritis, a blend of medical therapies and lifestyle modifications can keep symptoms in check. Many people who have osteoarthritis are able to enjoy favorite activities with few if any restrictions when they follow appropriate measures to control future damage of the joints. Significant damage to the joint may require joint replacement.

Risk Factors and Preventive Measures

The primary risk for osteoarthritis is increased age. Osteoarthritis is uncommon in people under age 50. Early diagnosis allows early treatment, which helps prevent further deterioration of the involved JOINT. Because so many factors converge to establish osteoarthritis, there are no measures known to prevent it.

See also ANKYLOSING SPONDYLITIS; EXERCISE AND HEALTH; INFECTIOUS ARTHRITIS; REITER'S SYNDROME; RHEUMATOID ARTHRITIS; SPINAL STENOSIS.

osteochondrosis See OSGOOD-SCHLATTER DISEASE.

osteogenesis imperfecta A genetic disorder, commonly called brittle BONE disease, in which there are defects in the ways the body produces type 1 collagen, a fibrous protein that is the foundation of bone formation. As a result the bones lack proper structure and density and are highly susceptible to FRACTURE. The defective collagen may affect other structures in the body as well, notably the LUNGS. HEARING LOSS is also common. Most osteogenesis imperfecta is inherited though may occur as the result of spontaneous MUTATION.

There are four types of osteogenesis imperfecta:

- Type 1 osteogenesis is the most common. People who have type 1 disease generally reach normal height and have few obvious skeletal deformities. Type 1 osteogenesis imperfecta typically causes more fractures during childhood than in adulthood. Hearing loss is pronounced and begins early in childhood.
- Type 2 osteogenesis imperfecta is the most rare and the most severe. It produces numerous deformities of the SKELETON and often is fatal in infancy. The abnormal collagen formation also profoundly affects the lungs, causing significant BREATHING problems.
- Type 3 osteogenesis imperfecta produces obvious skeletal deformities. Fractures before birth are common; ULTRASOUND can detect them in the FETUS. Type 3 disease also affects the lungs and muscles. Hearing loss begins in early childhood and often becomes complete by ADOLESCENCE.

- Type 4 osteogenesis imperfecta is more severe than type 1 but less severe than type 3. Fractures are most common before PUBERTY. Hearing loss begins in early childhood and is often profound.

The bones of infants who have osteogenesis imperfecta are very fragile and may fracture with the slightest contact, even that of picking up or holding the infant. Nonetheless, touch and holding are very important for proper development. The health-care team can provide suggestions to minimize the risk for fracture. Treatment for fracture is generally conservative, targeting a balance between immobilizing the fracture long enough for it to heal and allowing normal MUSCLE function as quickly as possible. Physical activity helps strengthen muscles and bone, which in turn minimizes fractures. The most numerous fractures occur during childhood when the bones are growing and thus have lower mineral content. The risk for fracture is lifelong, however, and may increase in women after MENOPAUSE when BONE DENSITY naturally declines. There are as yet no treatments to overcome the collagen deficiencies of osteogenesis imperfecta.

See also GENETIC DISORDERS; INHERITANCE PATTERN.

osteomalacia Softening of the bones that most often occurs as a result of vitamin D deficiency or abnormalities in vitamin D METABOLISM that prevent mineral crystals from accumulating in the BONE tissue. Vitamin D is essential to bone remodeling and the bone's ability to draw calcium and other minerals from the BLOOD circulation.

Osteomalacia develops when there is insufficient mineralization of the osteoid, a collagen-based substance the osteoblasts (bone-forming cells) produce. Instead of hardening into the bone matrix, the osteoid simply accumulates within the bone. Other causes of osteomalacia include chronic LIVER disease, END-STAGE RENAL DISEASE (ESRD), hypophosphatemia (insufficient phosphorus intake or metabolism), fluoride toxicity, and excessive antacid consumption.

Symptoms of osteomalacia include

- bone PAIN, especially in the hips
- numbness or tingling around the lips
- MUSCLE weakness
- pathologic bone FRACTURE (fractures that occur with minimal trauma or spontaneously)

Bone biopsy provides the conclusive diagnosis. Treatment is usually intense vitamin D supplementation until bone mineralization returns to normal. Depending on the underlying cause of the osteomalacia, some people may also need to take phosphorus supplements. Most people recover fully with appropriate treatment.

See also ANTACIDS; CALCIUM AND BONE HEALTH; MINERALS AND HEALTH; OSTEOPENIA; OSTEOPETROSIS; OSTEOPOROSIS; RICKETS; VITAMINS AND HEALTH.

osteomyelitis An INFECTION of the BONE. Typically the infection starts elsewhere in the body and spreads through the BLOOD circulation to the bone, though may originate in the bone as a complication of surgery on the bone (such as open reduction of a FRACTURE or JOINT REPLACEMENT). Bacterial infection causes most osteomyelitis, though other pathogens such as fungi (yeast) may also be responsible. The long bones in the leg are the most common locations for osteomyelitis in children; osteomyelitis in adults tends to settle in the hip or pelvis.

Symptoms and Diagnostic Path

Symptoms of osteomyelitis include

- PAIN from the area of the infection
- swelling in the area of the infection
- FEVER
- generalized discomfort and sense of not feeling well

The diagnostic path begins with a comprehensive medical examination and PERSONAL HEALTH HISTORY to identify any recent infections, injuries, or surgeries. X-RAY may show the area of infection, though other imaging procedures such as bone scan or MAGNETIC RESONANCE IMAGING (MRI) often produce more complete information. Biopsy of the site confirms the diagnosis and can identify the responsible PATHOGEN. Blood tests such as complete

blood count (CBC) are likely to show elevated white blood cell (WBC) count and other changes in the blood when there is an infection present.

Treatment Options and Outlook

Surgical debridement (an OPERATION to clean pus and damaged tissue from the infected area) and ANTIBIOTIC MEDICATIONS administered intravenously are the first course of treatment for osteomyelitis. Once the infection is under control, the doctor may switch to oral antibiotics. The course of antibiotic treatment may extend six weeks or more, depending on how well the infection responds.

Infections in the bone are particularly hard to treat because the bone's blood circulation does not deliver antibiotic medications to the bone very effectively. The infection may cause an ABSCESS (pocket of pus) that in turn causes the death of bone tissue. When such a scenario unfolds, the osteomyelitis becomes chronic and may destroy considerable bone tissue. It may be necessary for the orthopedic surgeon to create a surgical wound over the site of the infection to clean it and irrigate the area.

Acute osteomyelitis that responds to antibiotic medication may heal without complications. Chronic osteomyelitis, particularly with abscess, may have a less favorable outcome with extended antibiotic therapy necessary for several months. Several surgical operations may be necessary to clean the infection site and prevent abscesses from forming. The surgeon may leave the wound open or insert a drain to facilitate HEALING. Long-term chronic osteomyelitis can cause permanent damage to the structure of the bone. When chronic osteomyelitis accompanies joint replacement, it may be necessary to remove the prosthesis until the infection heals. The treatment of last resort is AMPUTATION.

Risk Factors and Preventive Measures

People at particular risk for osteomyelitis are those who have DIABETES or who are on hemodialysis for END-STAGE RENAL DISEASE (ESRD). Trauma to the bone, such as open fracture or surgery, also increases the risk for infection. Prevention is not always possible, though using measures to appropriately care for wounds and respond to early symptoms such as pain can keep the infection contained enough for antibiotic therapy to be effective.

See also BACTERIA; FUNGUS.

osteopenia A preclinical circumstance of reduced BONE DENSITY. Doctors generally consider osteopenia to precede OSTEOPOROSIS. Osteopenia has no symptoms and is a diagnosis the doctor arrives at as a consequence of the person's BONE density score with radiologic (X-RAY based) bone density measurement. About 34 million Americans, mostly women at or beyond MENOPAUSE and men older than age 60, have osteopenia.

Osteopenia may result from various metabolic circumstances. The World Health Organization (WHO) defines osteopenia as bone density that is no greater than 2.5 standard deviations below normal bone density (reported as a T-score between –0.1 and –2.5). Conventional diagnostic methods establish a scale of bone density relative to that of a young person of the same gender at an age when bone density is at its peak.

Many people can restore bone density through RESISTANCE EXERCISE and increased calcium consumption. Doctors generally do not treat osteopenia beyond these measures but instead closely monitor bone density. Osteopenia is a warning sign for women approaching or beyond menopause, as bone density loss accelerates when estrogen levels in the body decrease. Lifestyle factors that contribute to osteopenia include physical inactivity, cigarette smoking, and excessive ALCOHOL consumption, all of which interfere with calcium transfer and other metabolic processes related to bone remodeling.

See also CALCIUM AND BONE HEALTH; ESTROGENS; EXERCISE AND HEALTH; LIFESTYLE AND HEALTH; OSTEOPETROSIS.

osteopetrosis A rare genetic disorder in which BONE remodeling is defective. Though the body builds new bone (osteoblastic activity), it does not adequately clear away old bone (osteoclastic activity). Consequently the bones become very dense though are also very brittle and vulnerable to FRACTURE. When symptoms are present early in childhood (infantile osteopetrosis), the outcome is very poor because the excessive bone structure

crowds out the BONE MARROW. BONE MARROW TRANSPLANTATION is at present the only successful treatment for infantile osteopetrosis but itself carries significant risk.

Adult-onset osteopetrosis is present from birth but does not cause symptoms until adulthood when the abnormalities of bone structure are advanced enough to become apparent. Many adults who have osteopetrosis do not have overt symptoms and discover they have the disorder when receiving treatment for another condition for which the doctor requests an X-RAY. X-ray provides definitive diagnosis as osteopetrosis has a distinct, characteristic presentation. There are no treatments for adult-onset osteopetrosis other than efforts to reduce the risk for fracture. Adult-onset osteopetrosis increases the risk for OSTEOMYELITIS (INFECTION of the bone), which is one of the common reasons people initially seek medical care.

See also GENETIC DISORDERS; INHERITANCE PATTERN; MUTATION; OSTEOMALACIA; OSTEOPOROSIS.

osteoporosis A condition of diminished BONE DENSITY (the extent of mineralization of the bones). Though some loss of mineralization is a normal process of aging, osteoporosis represents an accelerated loss that causes health problems. Osteoporosis weakens the BONE structure; increases the risk for FRACTURE; and may result in bone deformities, particularly of the spine. The spine and hip are most vulnerable to fracture. Osteoporosis typically affects women after MENOPAUSE, though may develop earlier in women who do not produce estrogen, and men age 75 and older. About 10 million Americans have osteoporosis, 80 percent of whom are women.

Osteoporosis appears to primarily affect women for two reasons: estrogen and body size. Researchers do not fully understand how estrogen protects bone health but they do know that when estrogen levels fall dramatically, as with menopause, bone demineralization accelerates. As well, women have inherently less body mass—bone mass and MUSCLE mass—than men. Some researchers theorize that bone demineralization takes longer to affect men because their larger skeletons can withstand a greater loss of calcium before becoming thin and weak.

Symptoms and Diagnostic Path

Early indications of accelerated bone loss include loss of more than ½ inch in height and development of kyphosis (hump in the middle of the back). However, these signs develop slowly and over considerable time, often several decades, which makes them less apparent. Health experts call osteoporosis a silent disease because there are few indications of its presence until it is well established. Often the first symptom of osteoporosis is an unexpected fracture. The wrist, spine, and hip are the most vulnerable sites for fracture. X-RAY shows a characteristic porous structure to the bones, demonstrating the loss of mineral content and bone mass. Bone density tests such as DEXA scan can detect demineralization before fracture occurs.

Doctors use a scale of relative percentage of bone loss to measure the severity of osteoporosis. The scale represents bone loss as a standard deviation (SD) from the accepted norm for optimal healthy bone mass. An SD value of –2.5 or greater (2.5 SDs below the norm) is diagnostic for osteoporosis. Testing facilities report this value as a T-score; the norm for comparison is the bone density of a young healthy person of the same gender. Another representation is the Z-score, which compares the person's bone density to that of the norm for others of the same age and gender. Some testing facilities report bone loss as a percentage; a –2.5 SD value represents about a 35 percent loss of bone density (bone mass is 65 percent of what it should be).

Treatment Options and Outlook

Weight-bearing and RESISTANCE EXERCISE is essential to stimulate bone remodeling activity. For established osteoporosis treatment focuses on decreasing the resorption of bone to increase bone mass. Several kinds of medications can achieve this effect. Among them are calcium and vitamin D supplements, estrogen supplements, bisphosphonates, PARATHYROID HORMONE supplement, CALCITONIN supplement, and selective estrogen receptor modulators (SERMs). Individual circumstances determine which treatment approaches are most appropriate.

Calcium and vitamin D The body's ability to absorb dietary calcium diminishes with advancing

age. As well, people tend to drink less milk and consume fewer dairy products, the primary sources of dietary calcium, as they get older. Most adults should take calcium supplements to get 1000 to 1200 milligrams of calcium daily combined with dietary calcium. Though calcium cannot restore bone structure that is already lost to osteoporosis, the bones need abundant calcium simply to maintain bone remodeling. Vitamin D is necessary for the body to absorb calcium.

Estrogen Before the 1990s doctors routinely prescribed hormone replacement therapy (HRT) for women going through and women beyond menopause. The prevailing belief was that HRT provided protection for women against CARDIOVASCULAR DISEASE (CVD) and osteoporosis. Extensive studies demonstrated that HRT provided no protection for HEART disease and in fact increased the risk for some kinds of CVD (notably STROKE) as well as some forms of cancer.

The findings regarding osteoporosis were not as definitive as expected. Estrogen does slow the loss of bone. However, its effect is most pronounced during the first three to five years after menopause and it does not stimulate production of new bone. Though doctors sometimes prescribe estrogen replacement (in combination with PROGESTERONE supplement for women who have their uteruses) for women who are at high risk for developing osteoporosis, other medications are often more effective with fewer risks.

Bisphosphonates Bisphosphonates are medications that block the activity of osteoclasts to resorb bone and calcium. Because these drugs are relatively new, doctors do not know their long-term consequences. Bisphosphonates can stop the progression of osteoporosis as well as prevent osteoporosis from developing in men and women who have high risk. However, bone loss resumes when the person stops taking the medication.

BISPHOSPHONATES TO TREAT OR PREVENT OSTEOPOROSIS

alendronate	clodronate
etidronate	ibandronate
pamidronate	risedronate

Parathyroid hormone and calcitonin Parathyroid HORMONE and calcitonin are natural hormones within the body that regulate bone remodeling. Parathyroid hormone stimulates osteoblast activity (new bone formation); calcitonin suppresses osteoclast activity. Taken as supplements, these hormones have similar actions. They are not as effective as the bisphosphonates, however.

Selective estrogen receptor modulators (SERMs) Women who are beyond menopause can take SERMs, sometimes called designer ESTROGENS, which have many estrogen-like actions in the body. As the name suggests, however, SERMs selectively target estrogen receptors so are not entirely the same as estrogen. Some SERMs, notably raloxifene, have an estrogen-like effect on bone remodeling without estrogen-like effects elsewhere in the body. SERMs stop bone loss but do not stimulate new bone tissue.

Risk Factors and Preventive Measures

Women over age 70 who are white or Asian and are thin have the greatest risk for osteoporosis. However, regardless of ethnicity women past menopause have increased risk for osteoporosis because of the loss of estrogen. Other risk factors for osteoporosis include long-term use of systemic CORTICOSTEROID MEDICATIONS (such as to treat AUTOIMMUNE DISORDERS or endocrine disorders), cigarette smoking, low calcium consumption, physical inactivity, excessive CAFFEINE consumption, and excessive ALCOHOL consumption.

COMPLICATIONS OF FRACTURE

Though fracture alone is a significant health concern, the complications of fracture can be life threatening. Fracture generates a high risk for BLOOD clots as well as for fat emboli—fragments of fatty tissue that the fracture dislodges and that make their way into the blood circulation. Blood clots and fat emboli can cause STROKE or HEART ATTACK, depending on where they lodge in the blood vessels.

Calcium and vitamin D supplementation in combination with weight-bearing or resistance exercise early in life, but particularly before demineralization becomes significant, is the most effective preventive treatment. Health experts believe nearly all osteoporosis is preventable. But as with other lifestyle-related health conditions,

prevention efforts must begin in childhood and continue through life. The most effective time to supplement calcium is when the body is building bone mass—before age 20.

See also AGING, MUSCULOSKELETAL CHANGES THAT OCCUR WITH; DIET AND HEALTH; EXERCISE AND HEALTH; HIP FRACTURE IN OLDER ADULTS; OSTEOMALACIA; OSTEOPENIA; SKELETON; SMOKING AND HEALTH.

P

Paget's disease of the bone A rare and sometimes hereditary condition in which the process of BONE remodeling sporadically accelerates. The new bone that forms to replace old bone has increased mass, enlarging the bone structure, though is weaker than normal bone. Paget's disease of the bone affects bones randomly throughout the body. Most often affected are the spine, hips, legs, and cranium (skull). Paget's disease of the bone is more common in people over age 40 and affects men and women about equally. Some researchers believe Paget's disease of the bone is genetic and other researchers believe a VIRUS activates it.

Symptoms and Diagnostic Path

It is not uncommon for someone to be unaware he or she has Paget's disease of the bone until several bone fractures occur. Other people have obvious abnormalities of the spine, bowed legs, and moderate to severe JOINT PAIN and bone pain. When there is family history of Paget's disease of the bone the doctor may look in that direction for diagnosis. When there is not, doctors tend to first explore more common causes for similar symptoms (such as OSTEOPOROSIS). The diagnostic path then becomes circuitous, and diagnosis may take quite some time.

BLOOD tests to measure the presence of an enzyme, alkaline phosphatase, suggest a disorder of bone growth when the enzyme is present. Alkaline phosphatase levels in the body rise whenever there is new bone growth activity. Though not diagnostically conclusive, elevated alkaline phosphatase further points in the direction of Paget's disease of the bone. COMPUTED TOMOGRAPHY (CT) SCAN and MAGNETIC RESONANCE IMAGING (MRI) can show the extent to which the dysfunctional remodeling affects bones throughout the body. The pattern of bone damage is characteristic.

Treatment Options and Outlook

Treatment for Paget's disease of the bone targets both bone loss and symptoms such as pain. Medications to slow bone resorption (osteoclast activity) help retain more normal bone structure. Among these medications are CALCITONIN and the bisphosphonates (alendronate, clodronate, etidronate, pamidronate, risedronate, and tiludronate). ANALGESIC MEDICATIONS and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), in over-the-counter or prescription products, may be necessary to relieve pain.

Risk Factors and Preventive Measures

The primary risk factor for Paget's disease of the bone is a family history, known or suspected, of the condition. Though there are no measures to prevent Paget's disease of the bone, early diagnosis offers the best opportunity to mitigate bone loss and other symptoms.

See also BONE CANCER; CALCIUM AND BONE HEALTH; GENETIC DISORDERS; OSTEOGENESIS IMPERFECTA; OSTEOMALACIA.

palmar fibromatosis See CONTRACTURE.

patellofemoral syndrome Pain at or around the patella (kneecap) that often is worse when walking or running downhill or going down steps. Many people also experience the same kind of pain when sitting with the knees bent for a prolonged time. Doctors believe patellofemoral syndrome results from a combination of factors that include anatomy (individual variations in the structure of the knee), biomechanics (the function

of the knee), and the kinds of activities the person conducts.

The more inactive an individual is, the more likely he or she is to develop patellofemoral syndrome. However, most doctors do not believe this condition is one of overuse. Some experts believe an imbalance of STRENGTH among the four parts of the quadriceps permits dysfunctional tracking of the patella, contributing to the syndrome. Most athletic activities that use the quadriceps, such as running and bicycling, strengthen the lateral (outer) muscles more than the medial, pulling the patella off track.

Symptoms and Diagnostic Path

The main symptom of patellofemoral syndrome is PAIN going down steps or downhill and when sitting for long periods of time with the knees bent (flexed). The characteristic and specific nature of these symptoms allow the doctor to make a straightforward clinical diagnosis. X-rays and other diagnostic imaging procedures are not necessary unless there is reason to suspect another reason for the symptoms.

Treatment Options and Outlook

Treatment often combines one of the NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve INFLAMMATION and pain with PHYSICAL THERAPY to strengthen the quadriceps, particularly the medial (inner) muscles of this group. Most people experience relief from this treatment approach within two weeks and can return to their regular activities, including most sports, in four to six weeks.

Risk Factors and Preventive Measures

Women, particularly those in their late teens and early 20s who are inactive, are more likely than men to develop patellofemoral syndrome. Researchers do not know why this is. Exercises to maintain balanced strength in the quadriceps MUSCLE appears to prevent further occurrences of symptoms. A soft knee brace that holds the patella in position may also help maintain proper tracking of the patella. Some athletic trainers advocate wrapping or taping the knee before participation in an athletic event, which accomplishes a similar purpose.

See also KNEE INJURIES.

physical therapy A therapeutic approach to maintain or improve the biomechanics of the body. Physical therapy employs many modalities (types of treatments) including passive and active range of motion exercises, THERAPEUTIC MASSAGE, hydrotherapy, therapeutic ULTRASOUND, heat and cold, strengthening exercises, FLEXIBILITY exercises, and balance exercises. In the United States physical therapy requires a doctor's prescription. The doctor may prescribe physical therapy for people recovering from serious injury, surgery, or STROKE. Physical therapy also is helpful for conditions of impaired motor function such as CEREBRAL PALSY and PARKINSON'S DISEASE.

See also OCCUPATIONAL THERAPY; QUALITY OF LIFE; STRENGTH.

plantar fasciitis INFLAMMATION of the FASCIA along the bottom of the foot (plantar surface). Fascia is a thin, tough sheet of connective tissue that covers and connects the muscles, tendons, and other connective tissue structures throughout the body. It becomes irritated and inflamed with overuse. Plantar fasciitis develops with repeated stretching of the plantar fascia such as may occur with extensive walking or prolonged standing on a hard surface such as concrete. People whose jobs require walking on hard surfaces, such as mail carriers and police patrol officers, are particularly vulnerable to plantar fasciitis. Excessive body weight contributes to the stress the plantar fascia experiences, as do overly flat shoes, exacerbating the inflammation.

The pain of plantar fasciitis is distinctly characteristic; the doctor usually makes the diagnosis on the basis of symptoms. The PAIN begins in the heel and is most significant when returning to the feet after being off of them for a while, such as when first getting out of bed in the morning or after an extended work break. Immediate ice to the area of pain helps suppress the inflammation; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) block the inflammatory response and relieve pain. Shoes with cushioned soles and insoles, shock-absorbing floor mats, and shoe orthotics to hold the foot in the best position for the individual are among the methods that reduce the risk for plantar fasciitis. Stretching exercises to loosen the fascia further relieve pressure. Most people recover from an

episode of plantar fasciitis within six to eight weeks. With appropriate preventive measures, many people are able to keep symptoms from returning.

See also LIGAMENT; MUSCLE; REPETITIVE MOTION INJURIES; TENDON; WEIGHT LOSS AND WEIGHT MANAGEMENT.

polydactyly Extra fingers or toes. Polydactyly may occur spontaneously and isolated (without apparent cause) or in conjunction with GENETIC DISORDERS such as PATAU'S SYNDROME (trisomy 13). Most often the extra digit is on the little finger or little toe side of the hand or foot, respectively, and is so rudimentary as to be functionless. Nearly always the doctor recommends removing the extra digit, which may be done with banding (the doctor places a band tightly around the base of a rudimentary digit, cutting off its BLOOD supply so it slowly withers and falls off) or as a surgical AMPUTATION.

See also AUTOSOMAL TRISOMY; SYNDACTYLY.

polymyositis A chronic condition of widespread INFLAMMATION of the muscles. The inflammation causes weakness and difficulty with everyday movements including walking, reaching for objects, bathing, and dressing. Polymyositis is a type of inflammatory MYOPATHY that many researchers believe is autoimmune in its origins. Other researchers believe polymyositis and other inflammatory myopathies develop after viral INFECTION or as side effects of cholesterol-lowering therapy with statin medications. Polymyositis has alternating periods of RECURRENCE and REMISSION that tend to be lifelong. Most people are age 50 or older when they develop the condition.

Symptoms and Diagnostic Path

The severity and range of symptoms vary among individuals as well as across episodes within the same person. Symptoms of polymyositis may include

- MUSCLE weakness throughout the body though most pronounced in the shoulders, upper arms, hips, and thighs
- both sides of the body equally affected
- JOINT PAIN
- fatigue
- difficulty swallowing

The diagnostic path includes BLOOD tests to detect antibodies and elevated enzymes that indicate muscle injury within the body. Muscle biopsy may show the inflammation within the sample of muscle tissue. Sometimes MAGNETIC RESONANCE IMAGING (MRI) presents a pattern of the inflammation's presence in the body. Because there are no conclusive diagnostic tests for polymyositis, the diagnostic journey can be arduous and frustrating.

Treatment Options and Outlook

Treatment for polymyositis is a combination of CORTICOSTEROID MEDICATIONS and IMMUNOSUPPRESSIVE MEDICATIONS, which work together to mitigate the IMMUNE SYSTEM's inflammatory response. Physical therapy for passive and active range of motion exercises helps maintain optimal joint function. Daily physical activity has similar effect. Polymyositis is a lifelong condition that, when symptoms are severe, can result in permanent disability.

Risk Factors and Preventive Measures

Because researchers do not know what causes polymyositis, there are no known measures to prevent its development. Early diagnosis and treatment offer the most effective approach for minimizing the course of the disease and reducing the seriousness of its symptoms.

See also ANTIBODY; AUTOIMMUNE DISORDERS; CHRONIC PAIN; QUALITY OF LIFE; SYSTEMIC LUPUS ERYTHEMATOSUS (SLE); VIRUS.

proprioception The body's sense of its location within its physical environment. Proprioceptors are specialized molecules on PERIPHERAL NERVES in the muscles that send a continuous barrage of NERVE impulses to the basal ganglia and other structures of the BRAIN that have roles in balance and movement. The balance functions in the vestibular structures of the inner EAR also contribute sensory information. Proprioception is essential for all voluntary movement. Proprioception diminishes in neuromuscular disorders such

as PARKINSON'S DISEASE and also with ALCOHOL intoxication. The classic field SOBRIETY test is a measure of proprioceptive loss.

See also VESTIBULAR NEURONITIS.

prosthetic limb An artificial arm, hand, leg, or foot that provides functional replacement for an amputated or missing limb. A prosthesis represents a balance between function and presentable appearance. Prosthetic limbs available today can provide a very high level of function, allowing many people to return to nearly the same lifestyle as before the amputation.

Selection and fitting of the prosthesis can take place as soon as the AMPUTATION stump heals from the surgery. The prosthesis must attach firmly to the amputation stump, which is more difficult with high amputations (shoulder or hip). Factors that are important to consider include comfort and durability of the prosthesis. Most often it is advantageous to begin using the prosthesis as soon as possible after the amputation, to return to normal daily living.

There are numerous designs and styles of prosthetic limbs; the prosthesis is fitted to the person to meet the person's unique individual needs. Some prosthetic limb designs, particularly upper extremity, strive to appear as natural as possible. Other designs are primarily functional. Some designs are mechanical and others are electronic. Some prostheses are for specific purposes, such as athletic activities (running, hiking, bicycling, downhill skiing). Other prostheses may be more oriented toward allowing the person to return to a particular occupation or skill.

See also OCCUPATIONAL THERAPY; QUALITY OF LIFE.

R

Reiter's syndrome An inflammatory disorder commonly associated with INFECTION by the MICROBE *Chlamydia trachomatis*. Other pathogens that cause GASTROENTERITIS or SEXUALLY TRANSMITTED DISEASES (STDS) may also be responsible. Reiter's syndrome involves three components: URETHRITIS, reactive arthritis (arthritis that develops in reaction to infection elsewhere in the body), and CONJUNCTIVITIS. People who have Reiter's syndrome often have the human leukocyte antigen (HLA) B27, which is also associated with the autoimmune arthritis ANKYLOSING SPONDYLITIS. Some people develop INFLAMMATION of the AORTA and other major arteries as a consequence of the involvement of vascular connective tissue.

Symptoms and Diagnostic Path

Any of the three components of Reiter's syndrome may appear first, though commonly the urethritis is the first to manifest symptoms. The other two components generally appear within 28 to 35 days of the first component. Symptoms typically include

- general feeling of malaise
- low-grade FEVER
- MUSCLE aches and soreness, particularly when resting
- burning, itchy eyes
- conjunctivitis or IRITIS
- inflammation of the TENDON insertion point in affected joints (a unique arthritic symptom)
- genital discharge and painless, shallow ulcers

The diagnostic path includes laboratory testing for CHLAMYDIA in urethral and genital discharges as well as any fluid the doctor aspirates (withdraws with a needle and syringe) from affected joints. X-RAY studies may show characteristic changes in the affected joints.

Treatment Options and Outlook

The mainstay of treatment for Reiter's syndrome is therapy with NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). NSAIDs, usually prescription forms, control both inflammation and PAIN. An active bacterial infection requires treatment with the appropriate ANTIBIOTIC MEDICATIONS. Symptoms tend to last three to six months in most people; sometimes longer. In about a third of people, the arthritis component becomes chronic. Two thirds of people fully recover without residual effects.

Risk Factors and Preventive Measures

Men who develop Reiter's syndrome outnumber women about 10 to 1. Sexually transmitted chlamydia infection is the most common cause of the syndrome, so measures to reduce exposure to STDs can significantly reduce the development of Reiter's syndrome.

See also BACTERIA; HUMAN LEUKOCYTE ANTIGENS (HLAS); INFECTIOUS ARTHRITIS; PATHOGEN; SEXUAL HEALTH.

repetitive motion injuries Soft tissue injuries that occur as a result of overuse or performing the same motion over and over. Repetitive motion injuries, sometimes called cumulative trauma injuries, may occur as occupational injuries or ATHLETIC INJURIES. The most common repetitive motion injuries are TENDONITIS (INFLAMMATION of a TENDON) and BURSITIS (inflammation of a BURSA). These injuries may develop near any JOINT though are most common in the knees, hips, wrists, elbows, and shoulders.

Typical symptoms of repetitive motion injuries are

- PAIN and swelling
- numbness or tingling
- limited range of motion or movement

When establishing the diagnosis the doctor pays particular attention to the personal history of work, recreational, and other activities the individual performs on a regular basis. Diagnostic imaging procedures are usually not necessary. Treatment is rest from the activity that caused the symptoms in combination with NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); heat or cold to the site; and PHYSICAL THERAPY to learn stretching exercises and techniques for lifting, standing, and sitting that support musculoskeletal health.

Poor posture, staying in one position for an extended time, and repeating the same motion without breaking from it are the key risks for repetitive motion injuries. Prevention efforts include frequent changes in posture and position and frequent, short breaks from the repetitious task. This may be as simple as switching hands to perform the task or pausing at regular intervals to stretch the muscles, stomp the feet, roll the neck and shoulders, and shake or wiggle the hands.

See also CARPAL TUNNEL SYNDROME; OCCUPATIONAL HEALTH AND SAFETY; PATELLOFEMORAL SYNDROME; PLANTAR FASCIITIS; ROTATOR CUFF IMPINGEMENT SYNDROME; SYNOVITIS.

rhabdomyoma A benign (noncancerous) tumor that originates in MUSCLE tissue, usually skeletal muscle. Rhabdomyoma is somewhat more common in children than adults. The doctor may choose to surgically remove the rhabdomyoma to obtain a definitive diagnosis and rule out cancer. However, rhabdomyoma does not become cancerous. Rather, it may have the appearance of a cancerous tumor so the doctor removes it for biopsy and laboratory analysis. Rhabdomyoma may occur in the HEART, presenting a potentially life-threatening situation that usually requires surgery to remove the tumor.

See also LIPOMA.

RICE The acronym for rest, ice, compression, and elevation. RICE is the common first-line therapeutic approach for most musculoskeletal injuries such as SPRAINS AND STRAINS. Rest removes the injured part from the source of the injury. Ice slows the process of INFLAMMATION and eases PAIN. Compression, such as a wrap or brace, provides support so the muscles can relax. Elevation slows the flow of BLOOD through the part, further easing pain, reducing swelling, and enforcing rest.

See also ATHLETIC INJURIES; BURSITIS; FRACTURE; SYNOVITIS; TENDONITIS.

rotator cuff impingement syndrome A chronic overuse condition involving the rotator cuff, a group of muscles and tendons in the shoulder that stabilizes the shoulder JOINT—the glenohumeral joint where the humerus (long BONE of the upper arm) joins the upper part of the scapula (shoulder blade)—during elevation of the arm. The rotator cuff is vulnerable to strains ranging in severity from minor stretching of the tissues to significant tears. The resulting INFLAMMATION constricts, or impinges, the ability of the shoulder to move through its full range of motion. OSTEOARTHRITIS may also inflame the joint with the same consequence.

The doctor's examination includes a series of movements designed to elicit specific results that are relatively conclusive for rotator cuff impingement. However, other conditions can produce similar symptoms. COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), or ARTHROSCOPY may be necessary to confirm the diagnosis.

Most rotator cuff impingement symptoms respond to conservative treatment that includes hot or cold to the shoulder, NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), injection with CORTICOSTEROID MEDICATIONS, PHYSICAL THERAPY, and rest with limited exercises to maintain FLEXIBILITY and function of the joint. ADHESIVE CAPSULITIS, in which the tissues fuse together within the joint, is a major risk of immobilizing the shoulder. Though most people recover from an episode of symptoms without residual complications, rotator cuff impingement syndrome tends to be chronic, with repeated aggravation setting off new cycles of symptoms.

See also ATHLETIC INJURIES; MUSCLE; REPETITIVE MOTION INJURIES; SPRAINS AND STRAINS; TENDON.

ruptured disk See HERNIATED NUCLEUS PULPOSUS.

S

sciatica Irritation and INFLAMMATION of the sciatic NERVE, which runs from the lumbar spine (low back) down the buttock and into the leg. Sciatica is a type of peripheral NEUROPATHY that is often a chronic condition. Injuries to the hip and pelvis may involve the sciatic nerve. However, often there is no identifiable cause for sciatica.

The main symptom of sciatica is a shooting or searing PAIN that extends through the buttock and into the leg. Sciatica usually involves only one side of the body though sometimes symptoms are bilateral (involve both sides), depending on the cause. Typically no particular incident sets off the pain; it just occurs and may be severe. Sciatica may also interfere with foot placement or walking.

The diagnostic path begins with a NEUROLOGIC EXAMINATION that focuses on the lower body. In sciatica the reflexes at the knee and heel (ACHILLES TENDON REFLEX) are often slow or absent. Diagnostic procedures such as electromyogram (EMG) and nerve conduction studies typically produce abnormal results as well. Treatment targets the cause of the sciatica when known and symptoms otherwise. Medications such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) can relieve inflammation and pain, though people who have severe pain may need prescription ANALGESIC MEDICATIONS for pain relief. Exercises and physical activity to strengthen muscles and improve FLEXIBILITY are helpful when the inflammation subsides. Most sciatica is a long-term, chronic condition that comes and goes. Specific movements or activities may trigger pain in some people, and in other people the pain appears without apparent provocation.

See also DIABETES; HERNIATED NUCLEUS PULPOSUS; SPINAL NERVES; SPINAL STENOSIS.

scoliosis An abnormal curvature that takes the spine to the side. The healthy spine does not curve to the side. Scoliosis is idiopathic—that is, doctors do not know what causes it. Treatment to straighten the spine in childhood is important because the curvature is likely to become more extreme in adulthood and can interfere with various functions, including BREATHING. Scoliosis screening among children in the public schools is common in the United States. Adult-onset scoliosis, though uncommon, may occur with OSTEOPOROSIS, RHEUMATOID ARTHRITIS, and other inflammatory conditions that affect the spine.

Symptoms and Diagnostic Path

The distinguishing symptom of scoliosis is an S-shaped curvature seen in the spine from behind. Subtle symptoms of scoliosis that can help detect the condition before the curvature becomes pronounced include

- shoulders or hips that are noticeably uneven in height
- the tendency to lean to one side
- the appearance of a twisted or uneven waist
- shoulder blades that protrude prominently from the upper back
- complaints of backache or shoulder discomfort

The diagnosis of scoliosis is generally clear from physical examination, though the doctor may conduct X-RAY studies of the back to confirm it.

Treatment Options and Outlook

Treatment for scoliosis includes exercises to stretch and strengthen the structures of the back and often a brace that holds the spine in a more erect

posture. A child may need to wear a scoliosis brace only at night or all the time, depending on the severity of the scoliosis. Severe scoliosis or scoliosis that persists despite treatment may require surgery, in which the surgeon realigns the vertebrae, sometimes bracing them with steel or titanium rods to maintain them in proper position. Most scoliosis, when detected early, responds very well to treatment and is gone by the time the child reaches late ADOLESCENCE.

Risk Factors and Preventive Measures

Because doctors do not know what causes most scoliosis, there are no known risk factors or preventive measures. Scoliosis often accompanies other conditions such as CEREBRAL PALSY, MUSCULAR DYSTROPHY, and SPINA BIFIDA. Health experts urge women of childbearing age to take folic acid supplements, which can prevent many NEURAL TUBE DEFECTS such as spina bifida. It also tends to run in families, leading doctors to suspect there are hereditary factors at play.

See also KYPHOSIS; LORDOSIS; SURGERY BENEFIT AND RISK ASSESSMENT.

skeletal dysplasia Dysfunctional growth of the SKELETON such that the person is of significantly short stature. There are numerous forms of skeletal dysplasia, commonly and collectively called dwarfism, most of which are hereditary. Skeletal dysplasia may also occur as a result of HORMONE deficiencies during childhood. Each type of skeletal dysplasia presents characteristic symptoms. In general, skeletal dysplasias result in extremely short stature. The structures of the skeleton are nearly always disproportionate. Disorders of growth that are metabolic cause proportionate smallness. HORMONE THERAPY may increase skeletal growth when the cause is endocrine or metabolic. There are no treatments to alter the skeleton when the cause of the dysplasia is genetic.

See also ACHONDROPLASIA; GENETIC DISORDERS; INHERITANCE PATTERN; OSTEOGENESIS IMPERFECTA; RICKETS; SCURVY.

skeleton The organization of the bones in the body. The skeleton has two primary organizational divisions: the axial skeleton and the appendicular skeleton. The axial skeleton consists of the bones that form the body's axis or perpendicular line, which include the head, rib cage, and spine. It contains 80 bones. The remaining 126 bones—arms, hands, legs, feet, shoulders, pelvis, hips—form the appendicular skeleton.

The primary functions of the skeleton are to give the body structure, support and protect the body's internal organs, and enable mobility. Within certain bones is the BONE MARROW, which produces the body's BLOOD cells. The skeleton also serves as the body's "calcium bank," storing calcium when levels in the blood circulation are adequate and pulling calcium from the bones when blood levels of calcium drop too low.

For further discussion of the skeleton within the context of the structures and functions of the musculoskeletal system, please see the overview section "The Musculoskeletal System."

See also BONE; CALCIUM AND BONE HEALTH; OSTEOMALACIA; OSTEOPOROSIS.

sprains and strains Acute, traumatic injury to muscles, tendons, and ligaments, typically as a consequence of rapid and unexpected stretching such as may occur with a stumble, sudden twisting movement, or fall. A sprain is an injury to a LIGAMENT; ligaments connect bones to each other. A strain is an injury to a MUSCLE or TENDON; tendons extend from muscles to connect them to bones. Sprains and strains nearly always occur in or near joints. A muscle, tendon, or ligament may rupture (tear completely) under the force of a sudden stretch. Though immediate treatment—RICE (rest, ice, compression, elevation)—remains the same, a rupture may later require surgical repair.

A severe strain or sprain often is difficult to distinguish from a FRACTURE and should be treated as a fracture until medical assessment determines it is not.

Symptoms and Diagnostic Path

The main symptoms of a sprain or strain are PAIN and swelling following a sudden movement that involves a JOINT. Both are often immediate, and it may be difficult to use the limb. Grade 1 sprains and strains are painful but minor and do not necessarily require a visit to the doctor. However, it is

not possible to look at an injury and know whether there is a FRACTURE. A doctor should evaluate any injury in which

- it is difficult to bear weight or use the arm or hand
- there is numbness or tingling beyond the point of the injury (in the foot with an ankle injury, for example)
- pain is severe though the injury looks minor

Grade 2 injuries seldom require diagnostic imaging, though the doctor may request X-RAY, COMPUTED TOMOGRAPHY (CT) SCAN, OR MAGNETIC RESONANCE IMAGING (MRI) when there is doubt as to the severity of the injury because this can affect the treatment approach. Doctors assign a grade value to a sprain or strain to identify its severity, with grade 1 the least and grade 4 the most severe. ARTHROSCOPY may be necessary to accurately distinguish a grade 3 from a grade 4 injury.

Grade of Sprain/Strain	Severity of Injury
grade 1	stretching and minor tearing of fibers but structure remains intact
grade 2	partial tear of the structure and some instability of the JOINT
grade 3	significant tear of the structure and major instability of the joint
grade 4	complete tear of the structure and inability to use the joint

Treatment Options and Outlook

Grade 1 and grade 2 sprains and strains heal in two to six weeks with conservative treatment that includes continued RICE: rest, ice (or heat, after 48 hours, if heat feels better than ice), compression (elastic wrap, soft splint, tape, or brace), and elevation of the injured body part. Some grade 3 and nearly all grade 4 sprains and strains require surgery to repair the damage and reconstruct the tissues. The doctor can do this repair during diagnostic arthroscopy or with arthroscopic surgery after confirming the diagnosis through other means. Recovery after surgery may take up to six months, depending on the location and severity of the injury.

Risk Factors and Preventive Measures

Though sprains and strains are often ATHLETIC INJURIES, they can occur during everyday activities such as walking or lifting as well as in MOTOR VEHICLE ACCIDENTS. Proper technique for sports, including WARM-UP, and for lifting can prevent many soft tissue injuries. Taping or bracing vulnerable joints such as ankles, knees, and wrists provides additional support.

See also ACCIDENTAL INJURIES; ANKLE INJURIES; HIP FRACTURE IN OLDER ADULTS; KNEE INJURIES; SURGERY BENEFIT AND RISK ASSESSMENT; WEAK ANKLES.

spasm A sudden, involuntary, and extended MUSCLE contraction. Muscle spasms generally last no longer than a few seconds and are quite painful. Spasms may involve skeletal or involuntary muscle. Muscle spasms of the pulmonary system may manifest as ASTHMA or bronchiospasms that, when severe, may interfere with BREATHING. Skeletal muscle spasms may result from overuse, extreme cold, or neuromuscular disorders. Heat, massage, and gentle stretching can relieve muscle spasms. WARM-UP before strenuous exercise and regular activities to stretch and strengthen the muscles help prevent muscle spasm.

See also CHARLEYHORSE; CRAMP; MYOPATHY.

spinal stenosis Narrowing of the vertebral channel, usually in the lower (lumbar) back, that compresses the SPINAL CORD or the spinal NERVE roots. The narrowing may develop as a consequence of osteoarthritic changes, the formation of BONE spurs, or a congenital defect in which the vertebral channel is unusually narrow to begin with. Symptoms of spinal stenosis are weakness or numbness in the legs, along with disturbances of gait (the mechanics of walking) and balance. There may also be low BACK PAIN and PAIN in the legs.

The diagnostic path typically includes comprehensive medical examination with full NEUROLOGIC EXAMINATION and diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN that can show dimensional views of the internal and external structures of the spine. Such views help the doctor determine the location and extent of the stenosis.

When diagnosis is early, conservative treatment such as exercises that extend the spine (bend the body forward) and medications such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) may reduce the causes of the stenosis enough to relieve the compression of the nerves. Heat, cold, and weight loss also help. Physical exercise that stretches and strengthens the muscles without compressing the spine, such as bicycling and swimming, improves the ability of the muscles to support the body and further relieves pressure on the spine.

When these measures do not relieve symptoms, surgery to widen the vertebral channel may be necessary to prevent permanent loss of function in the legs. Because the outcome of back surgery is less predictable than many other kinds of surgery, it is important to discuss and understand the expected benefits and potential risks of any OPERATION the doctor proposes.

See also BONE SPURS; CERVICAL SPONDYLOSIS; OSTEOARTHRITIS; SCIATICA; SPINAL NERVES; SURGERY BENEFIT AND RISK ASSESSMENT.

syndactyly Fingers or toes that are fused together by connective tissue. Sometimes the fusion is only SKIN (simple syndactyly) and other times the fusion involves MUSCLE, ligaments, and BONE (complex syndactyly). Syndactyly is present at birth and often indicates a genetic disorder with additional symptoms. Most commonly the fusion involves the third and fourth fingers or toes, though sometimes affects multiple fingers or toes. Treatment is typically to separate the fused digits surgically to allow full use of the hand or foot.

See also GENETIC DISORDERS; LIGAMENT; POLYDACTYLY; SURGERY BENEFIT AND RISK ASSESSMENT.

synovitis INFLAMMATION of the synovial membrane that lines the JOINT capsule of joints such as the hip and knee. Synovitis is common in RHEUMATOID ARTHRITIS, GOUT, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and INFECTION. Generally there is PAIN, often severe, and swelling due to fluid accumulation. The SKIN over the joint is often hot to the touch and red. The doctor may aspirate (withdraw with a fine needle) some fluid from within the joint to rule out INFECTION.

Most synovitis improves with NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); severe or recurrent synovitis may require injected CORTICOSTEROID MEDICATIONS along with a local anesthetic to relieve PAIN and reduce inflammation. The extent of improvement depends on the underlying cause. Unfortunately synovitis often becomes a chronic presence with rheumatoid arthritis. DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS), which slow the progression of rheumatoid arthritis, may lessen the symptoms of synovitis as well. When BACTERIA are present in the synovial fluid, treatment requires ANTIBIOTIC MEDICATIONS.

See also BURSITIS; TENDONITIS.

T

talipes equinovarus A CONGENITAL ANOMALY in which an infant is born with one foot or both feet deformed into the shape of a club, hence the common term for the condition, "clubfoot." The affected foot turns in and under at the heel, such that the top of the foot appears nearly upside-down. All the bones, muscles, and other connective tissues are usually present though deformed in structure.

The anomaly forms in the last part of the first trimester of PREGNANCY when the muscles, bones, and connective tissues develop. Researchers do not know what causes talipes equinovarus though believe it is a combination of environmental factors (such as the fetus's position in the UTERUS) and genetic factors. The condition must be corrected for the child to walk; treatment is most successful when it begins shortly after birth.

The current standard of treatment is progressive casting during the first months of life, typically with the cast changed each week to move the foot slightly closer to normal position and gradually stretch the foot's soft tissue structures (the Ponseti casting method). Often the doctor must cut the ACHILLES TENDON to allow it to lengthen so the foot may completely return to its normal position. When the foot finally reaches normal position, the doctor removes the casts and replaces them with a special brace that the child wears for two months. Some children require further bracing at night for another few months. After treatment, the foot looks and functions as normal.

See also BIRTH DEFECTS; BONE; GENETIC DISORDERS; MUSCLE.

teeth Calcified formations that grow from the gums in the MOUTH. The teeth are necessary for cutting, tearing, and chewing the food as well as for forming the sounds of language. A person develops two sets of teeth during his or her lifetime. The first set, the primary teeth, erupts around six months of age and remains in place until six or seven years of age. Then the permanent teeth begin to push through the gum and the primary teeth fall out. There are 20 primary teeth and 32 permanent teeth by adulthood. The last 4 permanent teeth, molars in the back of the mouth called the wisdom teeth, erupt through the gumline at age 18 to 20.

When a blow to the face knocks out a tooth, retrieve the tooth and put it in a plastic bag with ice. The dentist often can put the tooth back in place and the tooth will reroot.

The outer layer of the tooth, the enamel, is the densest, hardest substance in the body. Highly mineralized, enamel cannot replace itself when damaged. At the core of the tooth is one of the softest, the pulp. The pulp encases and nourishes the NERVE. Between the enamel and the pulp is a layer of calcified tissue almost as hard as BONE, the dentin. The tooth's root extends from the jawbone. The main health condition to affect the teeth is DENTAL CARIES, or cavities. A cavity is a hole through the enamel that allows BACTERIA to enter the tooth. The bacteria eat away at the tooth's inner structure until reaching the pulp, at which point the cavity causes PAIN. A dentist can plug a cavity with a resin filler to stop the process and preserve the tooth. Other health conditions that can affect the teeth include GINGIVITIS, PERIODONTAL DISEASE and traumatic injury.

See also HALITOSIS; GLOSSITIS; SIALADENITIS.

temporomandibular disorders A group of conditions in which there is INFLAMMATION and often degeneration of the temporomandibular JOINT, the large joint that connects the lower jaw (mandible) to the temporal BONE of the cranium. There are numerous possible causes for temporomandibular disorders, ranging from a CONGENITAL ANOMALY of structure (such as uneven bite) to OSTEOARTHRITIS and grinding the TEETH (bruxism).

Symptoms and Diagnostic Path

The symptoms of temporomandibular disorders include

- inability to fully open the MOUTH
- locking of the jaw when open
- clicking sounds or sensations when chewing
- PAIN in the temporomandibular joint
- chronic HEADACHE

The diagnostic path begins with a comprehensive examination of the head and mouth. Sometimes the doctor determines the cause is primarily dental, such as uneven bite, and refers the person to a dentist for evaluation and treatment. Deterioration and inflammation of the joint are medical problems the doctor can attempt to treat. X-RAY can show whether there is a misalignment of the joint structures or deterioration of the bones. There is usually no need for additional diagnostic procedures unless the doctor feels the need to rule out other causes for the symptoms.

Treatment Options and Outlook

Treatment for temporomandibular disorders may include medications such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve inflammation and pain, heat or cold to the joint, dental splints or other devices to realign the bite, and dental repairs, if necessary. Temporomandibular disorders tend to be chronic. Many people put up with the discomfort for a considerable time before seeking medical care, by which time joint deterioration or other problems may be serious. Treatment may take time to be effective. In rare circumstances, usually when injury or congenital anomaly causes a structural problem with the joint, surgery may be necessary.

Risk Factors and Preventive Measures

Stress is often a significant factor in the circumstances that contribute to temporomandibular disorders, particularly with bruxism and clenching of the jaw, which causes irritation of the muscles and other tissues in the joint area. Many people find their symptoms improve with a combination of direct treatment (such as NSAIDs and heat) and indirect approaches such as MEDITATION or other stress-reduction techniques. These measures can reduce MUSCLE tension.

See also CHRONIC PAIN.

tendon A tough, fibrous band of connective tissue that joins MUSCLE to BONE. A tendon originates in the muscle. Like muscle, tendons have a rich BLOOD and NERVE supply. At its other end the tendon inserts into the bone. Mineralization at the insertion point creates a contiguous flow of tissue from muscle to bone. The largest tendon in the body is the ACHILLES TENDON, which joins the muscles of the calf to the bone of the heel. The most common health conditions involving tendons are TENDONITIS (INFLAMMATION of a tendon) and tendon rupture (a tear in the tendon).

See also BURSA; LIGAMENT; PATELLOFEMORAL SYNDROME; ROTATOR CUFF IMPINGEMENT SYNDROME.

tendonitis INFLAMMATION of a TENDON. Tendonitis most often occurs as an overuse injury. Overuse causes the fibers of the tendon to stretch and tear, leaving microscopic injuries throughout the tendon. Occasionally calcium deposits develop in a tendon. The injury activates the IMMUNE RESPONSE, which in turn initiates the inflammatory response.

The main symptoms of tendonitis are PAIN at the tendon's insertion point on the BONE and swelling over the site. Tendonitis most commonly occurs at the wrist, elbow, shoulder, knee, ACHILLES TENDON, and heel. Within the first 24 hours, RICE (rest, ice, elevation, and compression) is the most effective therapeutic approach. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) help relieve PAIN and inflammation. Most tendonitis improves within 72 hours and completely heals in two to three weeks with appropriate treatment.

See also ACHILLES TENDON INJURY; ADHESIVE CAPSULITIS; EPICONDYLITIS; PATELLOFEMORAL SYNDROME;

ROTATOR CUFF IMPINGEMENT SYNDROME; SHIN SPLINTS; SYNOVITIS.

torticollis Extended contraction of the muscles in the neck, pulling the head down and to the side. Torticollis, also called wryneck, may be present at birth or acquired. Acquired torticollis may develop after injury to the nerves or muscles of the neck though sometimes the doctor is unable to determine the cause. Often the neck muscles are stiff. In addition to the altered posture of the head and neck, other symptoms of torticollis include HEADACHE and restricted ability to move the head.

The diagnostic path includes a comprehensive NEUROLOGIC EXAMINATION to rule out other possible causes for the symptoms, particularly in adults for whom the symptoms are new. Treatment aims to relax and lengthen the neck muscles on the affected side through PHYSICAL THERAPY as well as self-performed stretching and FLEXIBILITY exercises (for adults). Rarely, surgery is necessary to release the muscles. Baclofen, an anticholinergic medication that blocks neurotransmitters essential for MUSCLE contraction, provides relief for some people. MASSAGE THERAPY and sometimes cervical traction help acquired torticollis that becomes chronic. Early treatment usually corrects congenital torticollis.

See also CEREBRAL PALSY; NEUROTRANSMITTER; SPASM; TALIPES EQUINOVARUS.

PAIN AND PAIN MANAGEMENT

PAIN is an unpleasant, subjective sensation associated with numerous health conditions and circumstances. Pain specialists are physicians who have additional education and training in the treatment and management of pain. Pain specialists may be anesthesiologists, internists, neurologists, orthopedic surgeons, psychiatrists, or physiatrists.

The entries in this section, "Pain Management," are about pain and its treatment. Entries discussing health conditions for which pain may be a symptom appear in the system section appropriate for the condition.

The Mechanisms of Pain

Pain can be a potent symptom, pointing to a significant injury or disease process within the body. Pain can also be a measure of HEALING, marking the body's progress toward wellness. And pain can be an indicator of dysfunction, persisting when there is no apparent reason for its existence. At a primal level, pain is a sensory survival mechanism. It tells the body to rapidly move to avoid its source or cause. The SPINAL CORD conveys pain signals directly to several regions of the CENTRAL NERVOUS SYSTEM, such as the thalamus, that regulate the body's REFLEX responses.

The message of pain begins with specialized molecules, called nociceptors, that line the dendrites of peripheral neurons. Dendrites are branchlike networks that extend from a NEURON to capture electrical signals and convey them to the NERVE body, which focuses them into a more organized nerve impulse. Nerve impulses travel along chains of neurons (nerve fibers) until they reach the large nerve clusters, the dorsal ganglia, that feed into the spinal cord. The dorsal ganglia further sort and focus nerve impulses, blocking many from continuing to the BRAIN but allowing passage for others. At this point the pain messages transition from the PERIPHERAL NERVOUS SYSTEM to the central NERVOUS SYSTEM.

The first structure within the brain to receive the nerve signals of pain is the thalamus. The thalamus further filters the impulses and takes rudimentary action to address certain aspects of the pain response. It initiates reflex reactions for pain signals that require it, dissipates some impulses that it interprets as meaningless, and sends the remainder on to the cerebral cortex for more sophisticated interpretation. Neuron activity in the cerebral cortex determines how the person will perceive the pain—whether the signals are indeed pain and what it will feel like (sharp, dull, stabbing) and how intense it will be (mild, moderate, severe). Pain generally results in one of two actions: removing the involved body part from the source of the pain or limiting the movement of the body part.

Traditions in Medical History

For thousands of centuries people have used natural substances to relieve pain. Willow bark contains salicylic acid, the basis of aspirin. Oil of wintergreen (*Gualtheria procumbens*) also contains salicylic acid. Opium occurs naturally in the poppy species *Papaver somniferum*. The leaves of the coca plant (*Erythroxylum coca*) contain COCAINE. Many modern analgesics contain synthetic preparations or derivations of these potent pain relievers. Some substances ancient healers turned to for pain relief had very narrow margins of safety:

mandrake, henbane, and hemlock, among others. Today's pharmacopoeia recognizes these substances as dangerous poisons that have no therapeutic applications. Other approaches to pain relief before the 20th century included ALCOHOL and the literal "bite the bullet."

The first pharmaceutical preparation for pain relief was aspirin, which came into use at the end of the 19th century. Pharmaceutical preparations of OPIATES and other pain relievers soon followed. Dozens of ANALGESIC MEDICATIONS are now available that can effectively treat and often prevent pain along the full spectrum of severity.

Breakthrough Research and Treatment Advances

Research in the 1990s provided breakthroughs in knowledge and understanding of pain mechanisms and, accordingly, for new ways to provide pain relief. Researchers know, for example, that women and men experience pain differently, raising the probability that hormones play a key role in pain perception and tolerance. There are genetic factors that come into play as well, such as the function or dysfunction of the genes that regulate the production and activity of cytochrome enzymes. The LIVER produces these enzymes, such as CYTOCHROME P450 (CYP450) ENZYMES, that are integral to how the body metabolizes numerous medications, including analgesics. Understanding pain pathways has helped doctors understand how analgesics interfere with those pathways, allowing clinicians to select the analgesics with the highest likelihood for relieving the pain.

Researchers know, too, that the body releases numerous biochemicals after injury (traumatic or surgical) that influence how nociceptors perceive stimuli. The body also releases biochemicals such as endorphins and enkephalins that act at the levels of both peripheral nociceptors and central (spinal cord and brain) neuroreceptors. Research is under way to develop medications that stimulate release of endorphins and enkephalins as well as to target other mechanisms of the pain pathway to relieve pain with lowered risk of side effects.

A

acute pain PAIN that arises suddenly and is often intense or severe in its quality. Acute pain signals injury to the body resulting from trauma, surgery, or disease process that damages tissue. Acute pain is short lived (typically less than one month) and goes away when the condition causing it improves or goes away. Doctors may use the term EUDYNIA to identify acute pain. Pain that does not go away when the underlying cause improves becomes CHRONIC PAIN, or MALDYNIA.

Chest pain may indicate heart attack or pulmonary embolism and requires emergency medical evaluation.

People often describe acute pain as sharp, stabbing, or burning. Physical signs that accompany acute pain include

- rapid BREATHING (TACHYPNEA)
- rapid HEART RATE (tachycardia)
- elevated BLOOD PRESSURE
- clammy SKIN
- dilated pupils

Severe acute pain may cause loss of CONSCIOUSNESS; severe pain requires prompt or emergency medical evaluation. Chronic and terminal health conditions may also cause episodes of acute pain.

Treatment for acute pain is two-pronged, targeting the pain as well as the underlying cause. ANALGESIC MEDICATIONS are generally effective for pain relief. There are numerous types of analgesic medications; doctors often prescribe or recommend them in combinations that target the nature and sometimes the cause of the pain. For example, the NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) block the release of PROSTAGLANDINS, biochemicals the IMMUNE RESPONSE generates that activate both the inflammatory response and NERVE transmission of pain signals. Narcotic analgesics, such as morphine and oxycodone, bind to receptors in the brain, preventing the release of neurotransmitters. As a result the pain impulse cannot be transmitted and the brain does not perceive pain.

COMMON CAUSES OF ACUTE PAIN

ADHESIVE CAPSULITIS	APPENDICITIS
ATHLETIC INJURIES	BARRETT'S ESOPHAGUS
BONE SPUR	BURNS
BURSITIS	cancer
corneal ABRASION	CYSTITIS
DENTAL CARIES	DIVERTICULAR DISEASE
DYSMENORRHEA	EPICONDYLITIS
EPIDIDYMITIS	FRACTURE
GALLBLADDER DISEASE	HEADACHE
HERNIATED NUCLEUS PULPOSUS	HERPES ZOSTER
ILEUS	KNEE INJURIES
MASTITIS	NEPHROLITHIASIS
NEURITIS	ORCHITIS
OSGOOD-SCHLATTER DISEASE	OTITIS media
PANCREATITIS	PEPTIC ULCER DISEASE
PERICARDITIS	PERITONITIS
PLEURISY	SCIATICA
SHIN SPLINTS	SICKLE CELL DISEASE
SINUSITIS	SPRAINS AND STRAINS
STREP THROAT	SUNBURN
surgery	SYNOVITIS
TENDONITIS	URETHRITIS
wounds	

Nonmedication methods also provide relief from acute pain. Sometimes just resting the affected area calms irritation and discomfort.

Wrapping or bracing an injured JOINT or limb provides support during activity. Ice to the affected area soothes INFLAMMATION, slowing the release of prostaglandins and other biochemicals that stimulate the pain response. Heat and therapeutic massage help tight, stiff muscles relax and improves BLOOD flow to the HEALING area. Alternating heat and ice can provide substantial relief for musculoskeletal pain.

See also ANESTHESIA; DERMATOME; EYE PAIN; MASSAGE THERAPY; NEURORECEPTOR; PATIENT CONTROLLED ANALGESIA (PCA); TERMINAL PAIN.

aging, changes in pain perception that occur with The perceptions of PAIN and the responses to pain relief methods change across the spectrum of age. A long-held belief is that infants experience pain only in the most rudimentary fashion; current research shows that infants experience nearly the same range and nature of pain as do adults. They also have the capacity to remember pain experiences. Children of all ages have surprisingly sophisticated understanding of pain and pain relief. At the other end of the spectrum, for about a third of people over age 60 pain is a daily experience. But as the body ages its ability to respond to ANALGESIC MEDICATIONS and other approaches to pain relief changes. So does its ability to generate its own natural pain relievers, endorphins and enkephalins.

Pain in Infants and Children

Though an infant's NERVOUS SYSTEM continues to develop after birth, the mechanisms for nociception (stimulation of nerves to transmit pain signals to the CENTRAL NERVOUS SYSTEM) are capable of function at about 28 weeks of gestational age—12 weeks before a full-term delivery. Though infants under age 12 months cry when in pain and exhibit reflexive behaviors to avoid painful stimuli, it is difficult to determine the severity of the pain. Young children (ages 1 to 5 years) are able to assess the severity of their pain and convey this to caregivers. A common pain scale for young children is the Wong-Baker Faces Scale, which uses a series of smiling-to-frowning faces for children to describe how their pain feels. Other pain assessment scales make use of the child's physical behaviors and degree to which the child responds to comforting measures to help caregivers assess the level of pain the child is experiencing.

Because a child's body is not fully developed, it metabolizes medications differently from that of an adult's body. Analgesic medications to relieve pain thus have different therapeutic levels, durations of effectiveness, and toxic levels. Some analgesics have undergone clinical study to quantify their actions and side effects in children though many have not. Pediatric dosing for analgesics is sometimes imprecise and tends to err on the side of undertreating pain in children. Children who have significant or CHRONIC PAIN should receive care from pediatric pain specialists to ensure that they receive adequate pain relief.

Pain in the Elderly

The number of peripheral sensory receptors gradually diminishes with aging, affecting the PERIPHERAL NERVOUS SYSTEM's ability to detect pain and convey pain signals to the central nervous system. This can result in more serious injury before there is adequate stimulus to avoid the situation. An older person may experience scalding and damage to the SKIN from water that is too hot, for example, before nociceptors detect the danger. Sensory receptors, including nociceptors, are also more susceptible to dysfunction and may overrespond to stimuli, resulting in MALDYNIA.

Other changes that take place in the body affect the METABOLISM of drugs, which in many circumstances means that less of the medication is necessary to achieve the desired therapeutic effect. The body may take longer to clear the medication, meaning doses should be farther apart (such as every six hours instead of every four hours) or that the DRUG may more quickly accumulate to a level of toxicity. Changes in gastric acid production and STOMACH function make the lining of the stomach more vulnerable to damage from highly acidic products, increasing the risk of bleeding with acidic medications such as ibuprofen and aspirin. Because of this the American Geriatric Society recommends that most people over age 65 take acetaminophen as the first choice for mild to moderate pain relief.

Because older people are more likely to have health conditions that require regular medications,

the risk for ADVERSE REACTION, undesired side effects, and DRUG INTERACTION is high. Among those conditions are many that cause chronic pain, such as OSTEOARTHRITIS, SCIATICA, and gout, increasing the need for pain relief methods. It is important for the older person to receive adequate pain relief, especially from chronic pain, which sometimes means taking narcotic pain relievers. Health experts recommend methods that minimize the use of analgesic medications, such as MASSAGE THERAPY, heat and cold, ACUPUNCTURE, BIOFEEDBACK, and relaxation techniques such as MEDITATION. Regular physical exercise, such as walking, increases the body's production of endorphins and enkephalins, amino acids that function as natural pain relievers.

See also AGING, EFFECTS ON DRUG RESPONSE AND DRUG METABOLISM; ALTERNATIVE METHODS FOR PAIN RELIEF; EFFICACY; EUDYNIA; NARCOTICS; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); OVERDOSE.

alternative methods for pain relief Methods for treating PAIN (typically CHRONIC PAIN) that are outside the parameters of conventional approaches such as ANALGESIC MEDICATIONS. Among the more common alternative methods for pain relief are ACUPUNCTURE, BIOFEEDBACK, HYPNOSIS, CHIROPRACTIC, MAGNET THERAPY, and MASSAGE THERAPY. Herbal and botanical products may also bring relief from pain associated with specific conditions.

Acupuncture

In 1997 the US National Institutes of Health (NIH) released a consensus statement regarding acupuncture. The statement cites these circumstances in which studies demonstrate acupuncture's effectiveness in relieving pain: after dental surgery, menstrual cramps (DYSMENORRHEA), FIBROMYALGIA, myofascial pain syndrome, OSTEOARTHRITIS, chronic low BACK PAIN, CARPAL TUNNEL SYNDROME, HEADACHE, and tennis elbow. In the Eastern tradition, acupuncture works by unblocking the pathways of chi, the energy of life. In the Western tradition, researchers postulate that acupuncture acts on nociceptors and PERIPHERAL NERVES.

Biofeedback

Biofeedback allows a person to influence the perceptions and responses of certain body functions such as those related to pain. Many health-care centers provide biofeedback training; the person then uses biofeedback techniques when needed. Biofeedback is especially effective for helping avert the onset of migraine and MUSCLE tension headaches, relaxing tense muscles that contribute to muscle SPASM and pain, and relieving stress.

Hypnosis

Hypnosis is a state of deep relaxation in which a person is especially receptive to suggestions the hypnotherapist makes. These suggestions may include visualization and relaxation techniques to apply in specific circumstances, such as when feeling tense or that pain is starting. Some people are able to practice self-hypnosis, which is particularly helpful for stress reduction with chronic pain conditions.

Chiropractic

Chiropractic manipulation of the neck and back (spine) can relieve muscle tightness, improve FLEXIBILITY, and restore function. The foundation of chiropractic is realignment of the spine to restore balance to the body. Chiropractic care requires visits to a chiropractor; the number and frequency of visits depend on the health condition. Chiropractic manipulation is particularly effective for conditions such as chronic low back pain, chronic neck pain, REPETITIVE MOTION INJURIES, and other musculoskeletal pain. The chiropractor also teaches methods to minimize injury through proper posture, movement, and stretching.

Magnet Therapy

Magnetic energy affects the flow of fluids and electrolytes (salts) through the cells of the body. Though research studies show conflicting results as to the effectiveness of static magnets (magnets or magnetic devices worn on the body), pulsed electromagnetic therapy is an effective therapeutic method physical therapists and physiatrists use. Static magnets may provide a less intense effect. People who have implanted electronic devices such as a PACEMAKER should not use static magnets or have pulsed electromagnetic therapy because these treatments may affect the device's proper functioning by altering its electromagnetic field.

Massage Therapy

Therapeutic massage relaxes stiff muscles and increases the flow of BLOOD. These effects improve flexibility and movement, and bring pain-relieving chemicals (the body's own substances or medications in the blood circulation) to the area. Massage therapy is effective for many types of pain and helps relieve the emotional stress that often accompanies conditions of chronic pain.

Herbal and Botanical Remedies

Numerous herbal and botanical remedies have pain-relieving actions. Some are effective for specific discomfort, such as DONG QUAI for dysmenorrhea (menstrual cramps) and FEVERFEW for migraine headaches. These herbs appear to block the release of PROSTAGLANDINS, substances the body produces that cause INFLAMMATION. Research studies also support the effectiveness of CHONDROITIN and GLUCOSAMINE, chemical compounds that occur naturally in the body. These compounds block the actions of enzymes that destroy connective tissue. Taken as nutritional supplements, chondroitin and glucosamine may be as effective as NSAIDs for relieving the inflammation of osteoarthritis that causes pain. Herbal and botanical products for pain relief may interact with OVER-THE-COUNTER (OTC) DRUGS and prescription medications, notably NSAIDS.

Benefits and Risks of Alternative Pain Relief Methods

Some alternative pain methods can interact or interfere with conventional therapies the doctor prescribes or recommends. It is important to discuss alternative methods with the doctor to effectively integrate them with other therapeutic approaches and to minimize the risk for complications, including worsening of the condition or interactions with other methods.

See also CRANIOSACRAL MASSAGE; MEDICINAL HERBS AND BOTANICALS; MIND–BODY INTERACTIONS; OSTEOPATHIC MANIPULATIVE TREATMENT (OMT); REFLEXOLOGY; REIKI; SAME; YOGA.

analgesic medications Drugs, products, and preparations that relieve PAIN, often called pain relievers. Some kinds of analgesic medications, such as OPIATES and other NARCOTICS, solely relieve pain by acting on neuroreceptors in the brain. Other analgesics have multiple effects, such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which also relieve INFLAMMATION and FEVER, and acetaminophen, which also relieves fever. Other kinds of medications primarily prescribed for other therapeutic uses are effective for pain relief in certain pain syndromes. Some ANTIDEPRESSANT MEDICATIONS, antiseizure medications, beta-antagonist medications (beta-blockers), and calcium channel antagonists (calcium channel blockers) can provide relief from and often can prevent NEUROGENIC PAIN (pain arising from injury to nerves) and migraine HEADACHE.

Routes of Administration

Analgesic medications are available in numerous formulations for several different ROUTES OF ADMINISTRATION. The most common route of administration for analgesics is oral—pills, tablets, capsules, and liquids taken by mouth. Some medications absorb poorly through the gastrointestinal tract so are far more effective in other forms such as transdermal patch, suppository, and injection. Topical medications applied to the SKIN may relieve MUSCLE and JOINT pain. The choice of both the analgesic medication and its route of administration affects how rapidly and how completely the medication relieves pain.

Oral The processes of digestion—how much and what kinds of food are in the STOMACH and gastrointestinal tract as well as individual variations in the digestive process—affect how rapidly oral medications enter the BLOOD circulation. Most oral analgesics begin to have an effect within 20 to 45 minutes and stay in the bloodstream at a therapeutic level for two to six hours. Some long-acting formulations are effective for 12 to 24 hours.

Transdermal patch Some products are available in transdermal patches, small adhesive patches placed on the surface of the skin, which get the medication rapidly into the blood circulation via absorption through the skin. The transdermal patch is also effective for delivering sustained-release medication (medication that slowly absorbs over a planned period of time, often 48 to 72 hours).

Topical Topical medications are also applied to the surface of the skin though are not absorbed

into the blood circulation to any significant extent. Topicals come as creams (water-based), ointments (oil-based), gels, sprays, and liquids. Topical analgesics may contain aspirin or other forms of salicylate, local anesthetic such as lidocaine (which numbs the skin's surface), hydrocortisone (an anti-inflammatory DRUG to reduce swelling at the skin's surface), and capsaicin.

Suppository Rectal suppositories package the medication in a soft, waxy capsule that, after insertion into the RECTUM, melts to release the analgesic. The rectal mucosa (mucous membrane lining of the rectum) has a rich blood supply that rapidly draws in the medication. Analgesics in suppository form are especially effective when nausea is a problem and for people who have difficulty swallowing.

Injection The more potent analgesics, notably narcotics, are poorly absorbed through the gastrointestinal tract and thus are available in injectable forms (shots). An injection may be

- intravenous (directly into a VEIN), which provides the most rapid (usually seconds) though short-term (30 minutes to 2 hours) pain relief
- intramuscular (into a muscle), which provides fast relief (within 10 minutes) that can last three to four hours
- subcutaneous (into the layer of fatty tissue beneath the skin), which provides prompt relief (within 20 to 30 minutes) but slower release of the medication into the blood circulation for analgesia that can last six to eight hours
- PATIENT-CONTROLLED ANALGESIA (PCA), in which intravenous medication flows steadily into a vein (intravenous administration) via a pump that regulates the amount of medication, either as at a preset rate or by patient demand (when the person presses the button to release more medication)
- continuous infusion of local anesthesia, which infiltrates tissue in a specific area with an anesthetic agent that relieves pain by numbing the nerves such as after a surgical OPERATION
- intrathecal analgesia, in which the pain specialist inserts a thin catheter into the space around the SPINAL CORD that delivers the analgesic in somewhat the same fashion as PCA

PCA and intrathecal analgesia offer highly effective pain control for ACUTE PAIN after surgery as well as severe pain due to chronic or terminal conditions. Continuous infusion of local anesthesia is especially effective after major surgery, reducing the amount of narcotic analgesics necessary to provide adequate pain relief. Continuous infusion of local anesthesia also allows greater comfort for coughing, deep BREATHING, and return to mobility, factors that are essential for HEALING as well as to prevent postoperative complications. Injections can cause discomfort and bleeding at the injection site.

How These Medications Work

Analgesic medications work by altering how the NERVOUS SYSTEM processes pain messages. They may

- raise the pain threshold (the point at which nociceptors perceive stimuli as painful); acetaminophen functions in this way
- block production of PROSTAGLANDINS and other biochemicals that sensitize nociceptors and activate the inflammatory response; NSAIDs function in this way
- bind with neuroreceptors in the BRAIN to alter the brain's interpretation of pain signals; opiates and other narcotics function in this way
- alter the balance of peripheral and central (brain) neurotransmitters; antidepressants and antiseizure medications function in this way
- change the ionization of cells to affect how molecules pass through them; beta blockers and calcium channel blockers function in this way

Taking analgesic medications properly is as important as the correct choice of drug when it comes to effective pain relief. Some analgesics need to be taken on a scheduled basis because they are more effective when they reach a steady THERAPEUTIC LEVEL in the blood. These medications generally provide sustained pain relief for short-term acute pain due to trauma or surgery and for long-term CHRONIC PAIN. Other analgesics are more effective when taken as needed, often indicated as "prn" in the doctor's instructions. These medications generally cover mild to moderate acute pain

and breakthrough pain with chronic conditions or during recovery from injury or surgery.

NARCOTICS AND ADDICTION

Many people, including doctors, are fearful of the potential for addiction with long-term use of NARCOTICS (OPIATES). However, numerous studies show that addiction is very rare, affecting fewer than 1 percent of people who take opiates for severe CHRONIC PAIN. Pain alters the mechanisms in the BRAIN that respond to opiates such that these mechanisms do not interpret the effect of the opiate as producing pleasure (a key factor in addiction). As well, addiction involves a combination of physical and emotional factors that typically are not present in severe pain. The unwarranted fear of addiction prevents many people from taking or receiving enough medication to relieve their pain.

Therapeutic Applications

Aspirin, acetaminophen, and over-the-counter NSAIDs are the most widely used medications in the United States. They have numerous therapeutic applications for mild to moderate relief from pain, inflammation, and fever. Doctors generally move to prescription medications when OVER-THE-COUNTER (OTC) DRUGS are not effective or when the nature of the pain is such that it exceeds their ability to provide relief (such as after surgery or significant injury). As knowledge and understanding about the mechanisms of pain grow, doctors are increasingly able to structure pain relief approaches that integrate different kinds of drugs for optimal effectiveness. The therapeutic application of many analgesics is highly individualized.

Risks and Side Effects

Risks and side effects vary according to the medication. It is possible to have an ALLERGY to any analgesic, creating the potential for HYPERSENSITIVITY REACTION. Though OVERDOSE is possible with any analgesic, it is a particular risk with aspirin, acetaminophen, and NSAIDs. People are more likely to self-medicate with these drugs and to take multiple products that contain these drugs as ingredients without recognizing the cumulative amount exceeds safety. These drugs also have a lower threshold for hepatotoxicity (damage to the LIVER) and renal toxicity (damage to the KIDNEYS), and can cause irreversible LIVER FAILURE or RENAL FAILURE even when taken at recommended dosage levels. Though many people worry about overdose with narcotics (opiates), it is far less of a risk. However, inappropriate use of narcotics has high risk for addiction. Aspirin and NSAIDs also are irritating to the gastrointestinal tract and may cause bleeding.

Medications such as beta-blockers, calcium channel blockers, and antiseizure medications have particular risks associated with these classifications of drugs. Though people taking these drugs for their primary intended purpose (cardiovascular conditions or seizure disorders, respectively) are generally well aware of these risks, people taking them for pain relief may not recognize warning signs of adverse reaction. It is important to weigh the potential benefits and risks of taking these drugs for pain relief. Analgesic medications also interact with numerous other medications, including OTC products and herbal remedies.

See also ALTERNATIVE METHODS FOR PAIN RELIEF; ANESTHESIA; NEURORECEPTOR; SCHEDULED DRUGS.

chronic fatigue syndrome A constellation of symptoms that exist within a framework of profound, persistent fatigue and generalized PAIN. Neither the fatigue nor other symptoms improve with rest. Chronic fatigue syndrome often debilitates those who have it and confounds the doctors trying to treat them. Researchers have as yet been unable to identify clear pathologic (disease process) reasons that account for the symptoms of chronic fatigue syndrome. Proposed causes include viral INFECTION (such as with EPSTEIN-BARR VIRUS or human herpesvirus 6), HYPERSENSITIVITY REACTION (ALLERGY), autoimmune disorder or other IMMUNE SYSTEM dysfunction, hormonal imbalance, chronic intermittent HYPOTENSION (low BLOOD PRESSURE), subclinical ANEMIA, and HYPOGLYCEMIA (low blood sugar). In many people chronic fatigue syndrome appears after a serious viral infection or after an event that causes significant stress.

Symptoms and Diagnostic Path

In many people, the initial symptoms of chronic fatigue syndrome are those of a viral infection such as INFLUENZA. But the symptoms do not go away after the typical timeline for such an infection. Because ongoing symptoms are widely variable and often without apparent physical cause, medical experts have established two basic criteria for a diagnosis of chronic fatigue syndrome. For six months or longer the person must have

- severe, chronic fatigue for six months or longer with diagnostic evaluation unable to find a medical reason for the fatigue
- four or more of the eight additional key symptoms: sore THROAT, MUSCLE pain, tender LYMPH nodes, noticeable difficulty with concentration and short-term memory; pain in numerous joints; headaches; difficulty sleeping or unrestful sleep; feeling of overwhelming exhaustion after physical exertion.

In addition to these core symptoms, most people have numerous other symptoms that may include

- ABDOMINAL PAIN
- CHEST PAIN and shortness of breath
- chronic COUGH
- NAUSEA, gastrointestinal discomfort, and DIARRHEA
- night sweats
- DEPRESSION, anxiety, or panic attacks
- jaw pain
- earaches
- "pins and needles" sensations
- dizziness

There are no diagnostic procedures that define chronic fatigue syndrome. Rather, the doctor orders certain diagnostic tests to rule out other potential causes for the symptoms. These include BLOOD tests to measure thyroid HORMONE levels, blood cell types and counts, electrolytes, globulins, and GLUCOSE levels in the blood circulation. The doctor may desire additional blood tests and urinalysis. Abnormal findings point in a different clinical direction; a diagnostic criterion for chronic fatigue syndrome is that such routine tests are normal.

Diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) and COMPUTED TOMOGRAPHY (CT) SCAN may rule out other suspected conditions though do not help the doctor

reach a diagnosis of chronic fatigue syndrome. Because the length of time the person experiences symptoms is a crucial element of the diagnosis, the diagnostic journey is often frustrating.

Treatment Options and Outlook

Because doctors do not know what causes chronic fatigue syndrome, treatment targets symptoms and is generally a combination of approaches tailored to the individual's responses and improvements. Treatment options include

- low-dose antidepressant medications, which may relieve pain as well as improve the quality of sleep
- antianxiety medications, which may relieve symptoms of anxiety, panic attacks, abnormal skin sensations, and dizziness
- antihistamine medications, which may relieve symptoms such as runny nose and nasal congestion
- modafinil, a nonamphetamine stimulant medication doctors commonly prescribe to treat narcolepsy, which improves alertness and cognitive function in some people who have chronic fatigue syndrome
- nonsteroidal anti-inflammatory drugs (NSAIDs), which may relieve joint pain and generalized discomfort
- daily physical activity at a level that is consistent but does not trigger a worsening of fatigue or other symptoms
- alternative methods such as acupuncture, biofeedback, massage therapy, craniosacral massage, hypnosis, Reiki, and therapeutic touch
- meditation, relaxation techniques, and stress-relief methods

Treatment often but does not always relieve symptoms enough to allow participation in the normal activities of living. For many people who have chronic fatigue syndrome, the fatigue is so overwhelming that it prevents virtually any level of activity despite treatment for other symptoms. Some people experience continued symptoms that wax and wane in severity. For most people who have the disorder, chronic fatigue syndrome is a long-term condition that does eventually improve or go away. The timeline for improvement is widely variable though typically spans several years. Many communities have support groups in which people who have chronic fatigue syndrome can share their experiences and concerns.

Risk Factors and Preventive Measures

Again because doctors do not know what causes chronic fatigue syndrome, there are no specific measures to prevent it. Doctors diagnose chronic fatigue syndrome in about four times as many women as men. For the most part chronic fatigue syndrome is relatively indiscriminate, affecting people across the spectrum of age and health status.

See also autoimmune disorders; cognitive function and dysfunction; fibromyalgia; generalized anxiety disorder; lymph node; quality of life; stimulants.

chronic pain Pain that persists longer than three months or beyond the point of healing for the condition that causes it. Chronic pain is very common, affecting the daily lives and activities of an estimated one in six Americans—about 60 million people. The most prevalent causes of chronic pain in the United States are low back pain, arthritis, and headache.

Pain experts differ in their definitions of what constitutes chronic pain. Research in the past decade has provided new understanding about the mechanisms of functional and dysfunctional pain. Some pain specialists view all chronic pain as dysfunctional because it no longer serves the purpose of warning the body. In this view the pain itself becomes the disorder, called maldynia, and treatment targets pain relief.

Other pain specialists consider some kinds of chronic pain (that which accompanies chronic health conditions such as rheumatoid arthritis) to remain symptomatic rather than dysfunctional. The pain persists because the underlying condition that causes it persists or progresses. In this view treatment targets the underlying condition, which often includes therapies to relieve pain as well as the pathology of the condition and its other symptoms. In rheumatoid arthritis, for example, treatment attempts to slow the inflammatory process

that causes degeneration in the joints as well as to relieve the pain of the degenerative changes.

Therapeutic methods for chronic pain typically combine various approaches to find those that are most effective for the individual. The subjective nature and diverse causes of chronic pain often mean effective relief comes through a process of trial and error. Generally lifestyle measures to maintain healthy body weight and optimal range of motion, such as daily physical exercise, are important for all types of pain. Exercise increases the body's release of endorphins and enkephalins, amino acid structures that act as natural pain relievers.

CONDITIONS IN WHICH CHRONIC PAIN IS COMMON

ANKYLOSING SPONDYLITIS	BURSITIS
CANCER	CARPAL TUNNEL SYNDROME
CERVICAL SPONDYLOSIS	CHONDRITIS
CHRONIC FATIGUE SYNDROME	chronic SINUSITIS
COMPLEX REGIONAL PAIN SYNDROME	EPICONDYLITIS
FIBROCYSTIC BREAST DISEASE	FIBROMYALGIA
GOUT	HIV/AIDS
INFLAMMATORY BOWEL DISEASE (IBD)	interstitial CYSTITIS
IRRITABLE BOWEL SYNDROME (IBS)	low BACK PAIN
migraine HEADACHE	myofascial pain syndrome
NEUROGENIC ARTHROPATHY	NEUROPATHY
OSTEOARTHRITIS	OSTEOMYELITIS
PATELLOFEMORAL SYNDROME	REPETITIVE MOTION INJURIES
RHEUMATOID ARTHRITIS	SCIATICA
SICKLE CELL DISEASE	spastic CEREBRAL PALSY
SPINAL CORD INJURY	TENDONITIS
UTERINE FIBROIDS	uterine prolapse
VAGINISMUS	VULVODYNIA

See also ACUTE PAIN; OSTEOARTHRITIS.

complex regional pain syndrome A chronic and often progressive condition of severe PAIN. There are two types of complex regional pain syndrome: type 1 (also called reflex sympathetic dystrophy), in which there is no identifiable NERVE injury, and type 2 (also called causalgia), which follows significant injury to a nerve. Type 2 is more common though the symptoms, treatment, and course of disease are similar for both types. Researchers do not fully understand the development and progression of either type of this syndrome but believe it results from dysfunction of the sympathetic NERVOUS SYSTEM, the functional division of the nervous system that regulates BLOOD flow. Complex regional pain syndrome is typically chronic (ongoing and long term) and often progressive (symptoms worsen over time). It most often develops in people who are between the ages of 40 and 60.

Symptoms and Diagnostic Path

The symptoms of complex regional pain syndrome typically involve a limb, with the arm being more common than the leg. In addition to pain, the course of disease causes pathologic (abnormal) changes in the SKIN, MUSCLE, connective tissue, and BONE. Early symptoms include

- severe burning pain that intensifies with slight touch, even that of a breeze (a nociceptor disturbance called allodynia)
- swelling in the affected arm or leg
- increased HAIR and nail growth
- dry, thin skin that alternates between warm and cool to the touch without influence from the external environment and may become cyanotic (bluish in color) or mottled (areas of irregular color)
- altered sweating (sometimes excessive, sometimes inadequate sweat production)

Symptoms change as the syndrome unfolds. Later symptoms include

- severe burning pain affects larger area of the limb
- diminished ability to move the limb
- decreased hair and nail growth
- permanent changes in the skin's texture and color (often becomes mottled)
- changes in bone structure and BONE DENSITY that are apparent on X-RAY
- TENDON contractions and muscle SPASM
- muscle atrophy (wasting of muscle tissue)

The diagnostic path is primarily clinical because the symptoms are fairly distinctive, particularly when there is history of traumatic or surgical injury to the involved limb. STROKE or HEART

ATTACK may also be a precipitating event. The doctor may use X-ray, bone scan, nerve conduction studies, and other procedures to assess the neuromuscular function of the limb. A comprehensive NEUROLOGIC EXAMINATION can rule out other possible causes of pain or complicating factors. However, there are no conclusive diagnostic procedures for this syndrome.

Treatment Options and Outlook

The earlier treatment begins, the better the outlook. Treatment may involve a blend of approaches, including

- anti-inflammatory medications such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) or CORTICOSTEROID MEDICATIONS to reduce INFLAMMATION and swelling
- tricyclic ANTIDEPRESSANT MEDICATIONS and antiseizure medications, which are often effective in relieving NEUROGENIC PAIN
- TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)
- NEURAL BLOCKADE (NERVE BLOCK) for pain that does not respond to noninvasive treatments
- RHIZOTOMY or sympathectomy (surgery to cut the nerve carrying the pain messages) for pain that does not respond to other methods of relief
- medications to prevent bone loss
- PHYSICAL THERAPY and MASSAGE THERAPY to maintain FLEXIBILITY and mobility
- heat or cold to sites of pain
- BIOFEEDBACK
- ACUPUNCTURE

Early treatment may arrest symptoms and prevent their progression. When the condition progresses, permanent damage to the limb becomes extensive and may render the limb useless. In severe cases the syndrome spreads to involve other parts of the body.

Risk Factors and Preventive Measures

Though doctors know that type 2 complex regional pain syndrome, the more common type, develops after significant trauma to the limb, they do not know what causes it to occur. Type 1 complex syndrome is even more baffling because there is no clear injury that precipitates symptoms. Accordingly, there are no measures known to prevent this disorder. However, early diagnosis and treatment can prevent the condition from progressing, limiting the extent of permanent damage that occurs.

See also LIVING WITH PAIN; MALDYNIA; QUALITY OF LIFE.

eudynia PAIN that exists as a symptom clearly associated with an underlying health condition or circumstance and results from stimulation of nociceptors (specialized sensors on the dendrites of neurons that convey pain messages). Eudynia, also called ACUTE PAIN, is typically short lived. Such pain is a common feature of injury and numerous disease processes and is the body's signal that something is wrong. Eudynia responds well to treatment with ANALGESIC MEDICATIONS and nonmedication methods such as rest, ice, compression (if appropriate), and elevation (if appropriate)—the RICE approach. ACUPUNCTURE and NEURAL BLOCKADE (NERVE BLOCK) are other methods that provide relief for pain due to traumatic injury or surgery. Eudynia resolves as the underlying condition improves.

See also ANESTHESIA; CHRONIC PAIN; MALDYNIA; NEURON; NOCICEPTOR.

headache PAIN perceived as coming from the face and head. Headache is a common experience, with about 45 million adults in the United States having frequent headaches. There are numerous types of headache resulting from various causes. Among them are tension headache, migraine headache, cluster headaches, sinus headache, and rebound headache. Headache may also indicate HYPERTENSION (high BLOOD PRESSURE), TRANSIENT ISCHEMIC ATTACK (TIA), or STROKE. Headache also is common with COLDS, flu, and FEVER. Very rarely headache may signal an INFECTION such as MENINGITIS or an ANEURYSM or a tumor in the BRAIN.

The nerves in the soft tissue of the head, neck, and face transmit the pain signals familiar as headache. There are no sensory nerves in the brain or bones of the skull, even though headache pain often feels as though it comes from deep within the head. Pain associated with events within the brain, such as tumor or stroke, arises from the increase in pressure within the cranium (enclosure of the skull) these conditions cause. The pressure stimulates the network of nerves that interlace with BLOOD vessels at the base of the brain. This NERVE and blood vessel network extends into the soft tissue surrounding the skull, magnifying the perception of pain.

Sudden, severe headache or headache with stiff neck, high or prolonged FEVER, or blow to the head may signal a medical emergency that requires urgent evaluation from a doctor.

Tension Headache

Tension headaches are the most common type of headache, resulting from MUSCLE tenseness in the shoulders, neck, and head. Stress, which often causes people to unknowingly tense their muscles, is a key factor. The stress may be emotional, related to job or family issues, or the stress may be physical, arising from lack of sleep, sitting too long in one position, going without eating, or loud noise. The tightened muscles aggravate nociceptors, the sensory molecules that respond to intense stimuli, which generate nerve signals of pain. The irritated muscles may also develop some INFLAMMATION, further stimulating nociceptors. Researchers believe biochemical factors, such as altered neurotransmitter balances (which affect the function of neurons) and increased production of PROSTAGLANDINS (which influence inflammation and changes in the walls of blood vessels), may also contribute to tension headaches by affecting the sensitivity of nociceptors. Tension headaches range in severity from mild discomfort to pain severe enough to cause NAUSEA, VOMITING, and disturbances of vision. Many tension headaches go away when the stressful situation ends. Others may last for several days or become chronic (recurring).

Migraine Headache

Migraine is the most common type of vascular headache. About 28 million Americans experience chronic migraine headaches. For many people the pain of migraine is debilitating. The conventional understanding of migraine is that the pain is a reaction to extreme changes (constriction and dilation) in the blood vessels that serve the head, likely as a consequence of rapid fluctuations in neurotransmitters, prostaglandins, and other substances that affect circulation. Recent research suggests there are genetic components to the mechanisms that regulate blood vessel constriction and dilation in the head, postulating that defects in genetic encoding (the protein messengers genes

send to cells that direct their activities) cause the abnormal vessel activity. Migraines tend to run in families, which supports the premise of genetic involvement.

There are two types of migraine:

- Classic migraine begins with an aura—a sensory experience, such as seeing flashing lights or smelling a particular odor that is not actually present, that portends the arrival of the headache. Disturbances of vision, confused thinking, and tingling in parts of the body such as the hands or feet may accompany the aura. Nausea and often vomiting may come next. Within about 30 minutes the pain erupts, often beginning on one side of the head or around the EYE. The pain may stay on one side of the head or spread to the entire head. A classic migraine lasts 24 to 48 hours.
- Common migraine lacks an aura though often there are vision disturbances, confusion, nausea, and vomiting before the headache starts. The pain may start on one side of the head and spread to both sides, or start with full involvement of the entire head. A common migraine may last three or four days.

Medications are the usual approach for recurring migraines. The most effective are those that prevent the migraine from unfolding. A class of drugs called triptans offering a new approach to migraine treatment became available in the early 1990s. Triptans (such as sumatriptan and zolmitriptan) work by binding with receptors on the cells in arterial walls that selectively constrict arteries, preventing the fluctuations in dilation and constriction that result in pain. The effectiveness of the different triptan products is highly individual, so often a period of trial and error is necessary to find the right match between person and drug. Triptans also have potentially severe side effects, including HEART ATTACK resulting from constricted CORONARY ARTERIES. People who have CARDIOVASCULAR DISEASE (CVD) such as CORONARY ARTERY DISEASE (CAD) or ISCHEMIC HEART DISEASE (IHD), or who have significant risk for CVD, should not take triptans.

Migraine headaches are most common in menstruating women, raising the probability of a hormonal connection. Some women have persistent migraines until pregnancy and then never have a migraine headache again. Other women develop migraines during pregnancy or after menopause. Oral contraceptives (birth control pills), which are hormones, also influence migraine headaches, improving them in some women and worsening them in others. The hormonal connection seems obvious but its precise nature remains elusive.

Cluster Headache

Cluster headache is a less common type of vascular headache in which a migraine-style headache recurs at about the same time of day for two to four months. The pain of cluster headache affects one side of the head and is typically severe. What will become a series of headaches begins suddenly, often around one eye. The involved eye becomes red and swollen, and the same side of the NOSE often becomes congested. Each headache lasts 30 to 90 minutes and then goes completely away. A person may go several months to several years between clusters. However, severe chronic cluster headache can occur in such a regular pattern that there is very little break between the end of one cluster and the start of the next. Cluster headache is more common in men and does not appear to have a hereditary component.

Sinus Headache

Sinus headaches result from the pressure of sinus congestion. The pain typically emanates from the front of the face, is more severe upon first waking and when tipping the head downward, and includes POSTNASAL DRIP among its symptoms. Sinus congestion may result from a cold, ALLERGIC RHINITIS (seasonal allergies), or sinus infection. The doctor should evaluate sinus headache that lasts longer than three weeks or when there a thick, green or yellow discharge accompanies the headache as these symptoms may indicate a bacterial infection that requires treatment with ANTIBIOTIC MEDICATIONS.

Rebound Headache

Rebound headache is an unpleasant circumstance that develops as a consequence of long-term use of analgesic medications (more than twice a week on a fairly regular basis) to treat chronic headache. The

headache improves or goes away with the medication but then returns when the medication wears off or the person does not take the medication. Eventually the medication can no longer relieve the headache and often the headaches become more frequent and more severe.

Treatment for rebound headache requires a shift to other methods for relieving pain, such as ACUPUNCTURE or BIOFEEDBACK. The doctor may also prescribe medications to prevent headaches, such as propanolol or isometheptene, and a triptan medication to thwart a migraine at its early warning signs (such as an aura). It may take several weeks to two months for the headaches to fully recede. Stress management methods such as MEDITATION and YOGA help shift focus to controlling and healing the pain rather than on the pain itself.

KEEP A HEADACHE JOURNAL

Doctors recommend people who have frequent headaches keep a journal that describes their symptoms in detail. This helps identify patterns for how the headaches develop and what effects various pain relief measures have to relieve the pain.

Symptoms and Diagnostic Path

The symptoms of headache provide important clues about the cause and potential treatment options. The doctor will want to know the following:

- How does the pain feel? Common descriptions of headache pain include sharp, dull, throbbing, stabbing, viselike.
- How does the pain start? Some headaches start as minor discomfort and increase to a level of pain that interferes with activities. Some headaches start suddenly with moderate to severe pain.
- Where is the pain? Headache pain may be primarily on one side of the head or face, involve the entire head and face, or involve only the face or only the head. The pain may feel like it encircles the head, is deep or along the surface of the scalp, or comes from a specific location.
- How long does each headache last and how often do headaches occur?
- To what extent does the headache interfere with regular activities?
- Are there any disturbances of vision (such as flashing lights or double vision), awareness, alertness, sensory perception, ability to speak, ability to move?
- Do there seem to be any particular triggers for the headache, such as stressful situations, specific foods, certain locations or activities?
- Are there other symptoms such as fever, sinus congestion, stiff neck, nausea, vomiting?
- What methods and medications have been tried to relieve the headache? Are they unsuccessful, sometimes successful, or partially successful?

The doctor will also ask questions about any other health conditions and whether other family members have chronic headache, migraine headache, seasonal allergies, and AUTOIMMUNE DISORDERS. The doctor typically performs a general medical examination including a basic NEUROLOGIC EXAMINATION and a basic OPHTHALMIC EXAMINATION. Imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN and MAGNETIC RESONANCE IMAGING (MRI) may rule out rare causes for headache such as stroke or tumor. However, the doctor often can make the diagnosis based on the symptoms and headache history.

Treatment Options and Outlook

Most treatment approaches for chronic headache combine medications and other methods to relieve symptoms when the headache occurs and prevent headaches from recurring. Relaxation techniques such as meditation and yoga can help lessen the effect of stress. Other methods in which the person learns to recognize indications that a headache is coming on are often effective in stopping the headache from unfolding. Biofeedback and HYPNOSIS may help a person halt a headache. Numerous prescription medications are available to prevent headaches.

Heat to the back of the neck and resting in a dark, quiet room are measures that often soothe headaches that do occur. Medication is the mainstay of treatment for headache once it develops. Aspirin, acetaminophen, and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen are

TYPES OF CHRONIC HEADACHES

Type of Headache	Characteristic Symptoms	Treatment Approaches
cluster	severe migraine-like PAIN on one side of the head or face nasal congestion on the affected side headache recurs, usually daily, for a period of weeks to months (a cluster) and then goes away for a period of time	medications and other methods to try to prevent the cluster of headaches medications and other methods to head off a headache as it is starting analgesics during the headache do not usually take effect quickly enough to be useful
migraine	aura (classic migraine) such as flashing lights or other sensory activation before the headache itself begins vision, sensory, and cognitive disturbances (classic and common migraine) moderate to severe pain often on one side of the head NAUSEA and VOMITING inability to participate in regular activities	rest in a quiet, dark room caffeine NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS): ibuprofen, naproxen beta-blockers: propanolol, atenolol calcium channel blockers: amlodipine, verapamil ergot derivatives: ergotamine, dihydroergotamine, ergotamine with CAFFEINE triptans: almotriptan, eletriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan antidepressants: amitriptyline, fluoxetine, nortriptyline, paroxetine, sertraline isometheptene NARCOTICS: injection of morphine for severe pain
rebound	headache that returns as soon as the medication taken to relieve it wears off	medications to prevent headache such as beta-blocker or isometheptene relaxation techniques and other nonmedication methods
sinus	pain along the cheek bones, around the eyes, in the jaw pain is worse upon first waking up in the morning and when tipping the head forward nasal congestion and postnasal drip	ANTIBIOTIC MEDICATIONS for INFECTION ANTIHISTAMINE MEDICATIONS for ALLERGIC RHINITIS decongestant spray or drops oral decongestant medications
tension	steady, pressure-type pain that comes on gradually often occurs during times of physical or emotional stress may go away when source of stress ends	over-the-counter analgesics: acetaminophen, aspirin, NSAIDs antidepressants: amitriptyline, fluoxetine, nortriptyline, paroxetine, sertraline relaxation and stress management methods frequent stretching and movement to change position ACUPUNCTURE MASSAGE THERAPY CHIROPRACTIC

often effective for relieving the pain of headache once it develops. Severe headache of any type may require narcotic analgesic medications to relieve the pain. The exception is cluster headache, for which preventive measures are more effective because the headache, despite the severity of its pain, generally lasts a shorter period of time than it takes for analgesic medications to achieve a therapeutic effect in the body. The herb FEVERFEW, available as an over-the-counter dietary supplement in the United States, is effective against migraines for some people.

Medication is also the mainstay of prevention for migraines and cluster headache, though prevention approaches are more effective for migraine than cluster headaches. Medications that may prevent migraines and cluster headache when taken on a regular basis include propranolol, methylsergide, amitriptyline, valproic acid, verapamil, and lithium carbonate. Triptans taken at the first indication of migraine are effective for many people in preventing the headache. Occasionally a doctor may give an injection of narcotic analgesic such as morphine. Sinus headaches may require treatment with antibiotic medications for infection or ANTIHISTAMINE MEDICATIONS for allergic rhinitis. Decongestant medications (nasal sprays, nasal drops, or oral forms) may help sinus headache of either type.

Risk Factors and Preventive Measures

Risk factors for headaches include physical and emotional stress, low blood GLUCOSE from missing meals, exposure to environmental irritants such as cigarette smoke, excessive CAFFEINE consumption, allergies or HYPERSENSITIVITY REACTION, foods that contain tyramines (such as red wine, smoked meats, and hard cheeses), and MENSTRUATION in women. Preventive measures include relaxation techniques and stress management methods, avoiding known or suspected factors that precipitate headache, and prophylactic (preventive) medication. The right combination of approaches can significantly reduce the frequency and severity of chronic headaches.

See also ACUPUNCTURE; LIVING WITH PAIN; NEURALGIA; NEURON; NEURORECEPTOR; STRESS AND STRESS MANAGEMENT.

L–M

living with pain Approaches and methods for improving QUALITY OF LIFE when PAIN is part of daily living. For one in five Americans, pain is a daily experience. Nearly 60 million people in the United States have OSTEOARTHRITIS, 45 million experience frequent headaches severe enough to interfere with regular activities (28 million of them have chronic or recurrent migraine headaches), and 5 million have chronic low BACK PAIN.

Living with pain requires an integration of medical and lifestyle methods. There are many kinds of ANALGESIC MEDICATIONS, some of which provide general pain relief and others that target specific kinds of pain. Research over the past 10 years has provided significant insight into the mechanisms of pain, resulting in new classifications of drugs that intercede at different junctions along pain pathways. ROUTES OF ADMINISTRATION such as transdermal patches (SKIN patches) or long-acting oral formulations can deliver a steady rate of pain medication, smoothing out the ups and downs that accompany other dosage forms such as short-acting tablets and pills. Though most people do not want to take medications on a regular basis, medications may be necessary to slow a disease process (such as RHEUMATOID ARTHRITIS) or to alleviate enough pain to allow participation in daily activities.

Daily physical exercise, such as walking, benefits nearly every condition in which there is pain. Physical activity stimulates the body to release endorphins, enkephalins, and other biochemicals that act as natural pain relievers or otherwise influence the body's inflammatory response and pain mechanisms. Regular activity also improves MUSCLE STRENGTH and JOINT FLEXIBILITY, helps maintain healthy body weight, and relieves stress. Alternative methods such as ACUPUNCTURE and CHIROPRACTIC can provide extended pain relief (days to weeks). BIOFEEDBACK, VISUALIZATION, and MEDITATION are additional methods for coping with and managing pain.

See also ACUTE PAIN; CHRONIC PAIN; EUDYNIA; HEADACHE; MALDYNIA; MASSAGE THERAPY; STRESS AND STRESS MANAGEMENT.

maldynia CHRONIC PAIN that exists without apparent organic or physical cause. The defining characteristic of maldynia is that the PAIN does not activate specific pain receptors (nociceptors) or follow conventional pain pathways. Some researchers believe maldynia represents a malfunction of the BRAIN's pain interpretation processes, likely an imbalance among brain neurotransmitters. Other researchers believe maldynia represents disturbances in the body's pain sensory mechanisms, perhaps changes at the level of the NEURON that alter the sensitivity of pain signals.

Maldynia is an extraordinarily frustrating condition. Beyond the limitations on enjoying life that continual pain imposes, there are the psychologic ramifications of the perception that the pain is not real. Doctors who are unfamiliar with chronic pain syndromes may be suspicious of reported pain without apparent cause that persists despite efforts to resolve it and may dismiss the person's symptoms as "psychosomatic" or emotional in its basis. Research suggests that though emotions influence pain perception, this occurs through biochemical and physiologic pathways in the body and the CENTRAL NERVOUS SYSTEM.

Symptoms and Diagnostic Path

The primary symptom of maldynia is pain that does not go away and has no apparent cause. Doctors do not generally consider chronic health conditions for which pain is a component, such as

OSTEOARTHRITIS, to be maldynia because the pain, though persistent and long-term, results from an identifiable cause. The pain associated with maldynia may be sharp or dull, burning or aching, generalized or focused, continuous or intermittent. The one constant no matter the nature of the pain is the absence of any pathologic reason for the pain to exist.

The diagnostic path differs for each individual, generally focusing on ruling out potential causes for pain. Diagnostic procedures that rule out particular causes of pain may include imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI), electromyelogram (EMG), evoked potential studies, and NERVE conduction studies.

Treatment Options and Outlook

Treatment for maldynia ranges from nonnarcotic and narcotic ANALGESIC MEDICATIONS to nerve block injections to alternative approaches such as ACUPUNCTURE and BIOFEEDBACK. For most people with maldynia, treatment is a process of trial and error with the goal of allowing participation in desired daily activities rather than complete relief from pain. Treatment is unique to the individual and varies over time, depending on effectiveness and improvement of the pain. Daily physical activity to the extent possible releases natural pain relievers in the body called endorphins. Exercise also improves balance, MUSCLE tone, and one's overall sense of well-being.

Maldynia is a life-altering condition. It interferes with nearly every aspect of life, and often is partially to completely disabling. Maldynia can persist for years, go through cycles of improvement and worsening, or suddenly disappear. The elusive nature of its symptoms makes maldynia a difficult challenge. However, with appropriate medical guidance and a positive outlook, many people are able to achieve a reasonable QUALITY OF LIFE. It is important to find a doctor who understands and has experience treating chronic pain syndromes, and to keep the faith that improvement is possible.

Risk Factors and Preventive Measures

Researchers continue to look for the reasons for maldynia. There does appear to be a correlation between maldynia and a preceding circumstance of untreated or undertreated ACUTE PAIN. Appropriate pain relief for acute pain (EUDYNIA) may prevent maldynia from following a significant trauma such as injury or surgery. Otherwise, there are as yet no clear risk factors and consequently no known measures to prevent maldynia.

See also ALTERNATIVE METHODS FOR PAIN RELIEF; NEUROTRANSMITTER.

TREATMENT OPTIONS FOR MALDYNIA

Over-the-Counter Medications	Prescription Medications	Injected Medications	Mechanical Approaches	Alternative Approaches
acetaminophen	NSAIDs: diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, meclofenamate, oxaprozin, piroxicam	TRIGGER-POINT INJECTIONS	MASSAGE THERAPY	ACUPUNCTURE
aspirin		NERVE blocks	PHYSICAL THERAPY	BIOFEEDBACK
NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS): ibuprofen, ketoprofen, naproxen		injectable narcotics	TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS)	exercise
topical analgesics	NARCOTICS: codeine, hydromorphone, levorphanol, oxycodone, oxymorphone	epidural blocks	heat/cold	hydrotherapy
topical counterirritants		epidural steroids	CHIROPRACTIC manipulation	MEDITATION
	antidepressants: selective serotonin reuptake inhibitors (SSRIs), tricyclics	intracathal injection	SPINAL CORD electrostimulation	self-hypnosis

N

neural blockade (nerve block) An injection of an analgesic medication into a NERVE to block the transmission of PAIN to the CENTRAL NERVOUS SYSTEM from a part of the body. Neural blockade is common as preventive analgesia for ACUTE PAIN following surgery or injury and sometimes effective for treatment of CHRONIC PAIN. The doctor may also use a neural blockade as a trial to determine the effectiveness of such an approach before conducting a permanent procedure such as RHIZOTOMY or NEUROLYSIS. The effects of neural blockade are temporary though generally long-lasting for most people (several weeks to several months, depending on the anesthetic agent). The doctor may inject a major nerve, such as the brachial plexus, or a spinal nerve. The most common sites for neural blockade include

- occipital and trigeminal nerves, which serve the face and head
- mandibular and maxillary nerves, which serve the jaw and lower face
- suprascapular nerve, which serves the shoulder
- brachial plexus, which serves the upper arm, neck, and side of the face
- femoral nerve, which serves the hip and femur (thigh)
- sciatic nerve, which serves the back of the leg and foot

The risk is slight for complications or adverse reactions. Bleeding and bruising at the site of the injection are fairly common and generally minor. Some people are allergic to topical anesthetics and may have a HYPERSENSITIVITY REACTION to a neural blockade. Unintended loss of sensation or movement along the nerve's pathway is also possible though uncommon.

See also ANALGESIC MEDICATIONS; CRANIAL NERVES; SPINAL NERVES.

neurolysis Destruction of part or all of a NERVE to prevent it from transmitting PAIN signals to the CENTRAL NERVOUS SYSTEM. Neurolysis generally becomes a treatment option for CHRONIC PAIN, or MALDYNIA, when other methods to control pain are unsuccessful. There are three major methods of neurolysis:

- Chemical neurolysis involves injecting a chemical into the nerve that destroys the NEURON bodies. Commonly used chemicals include phenol, ethyl ALCOHOL, and hypertonic saline.
- Surgical neurolysis involves cutting the nerve along the pain pathway that carries pain signals to the BRAIN.
- Ablative methods, primarily radiofrequency ablation (which uses heat) and cryoablation (which uses freezing), cause neurons to die.

The effects of neurolysis are permanent. Complications and risks include undesired loss of sensation, loss of movement (PARALYSIS), bleeding, incomplete pain relief, or worsened pain. The results of neurolysis vary among individuals and sometimes take several weeks to months to become fully effective. When neurolysis is successful, it ends the pain.

See also ANALGESIC MEDICATIONS; ALTERNATIVE METHODS FOR PAIN RELIEF; COMPLEX REGIONAL PAIN SYNDROME; NEURAL BLOCKADE (NERVE BLOCK); RHIZOTOMY; SURGERY BENEFIT AND RISK ASSESSMENT.

neurogenic pain PAIN that results from dysfunction of the nociceptors, specialized molecules on

the dendrites of neurons that detect pain and initiate transmission of pain signals to the CENTRAL NERVOUS SYSTEM. Neurogenic pain often follows an injury (traumatic or surgical) for which pain is a reasonable symptom. However, when the injury heals, the nociceptors can remain hypersensitive to stimuli, particularly touch and temperature, which they perceive as painful, and the nociceptors continue to initiate pain signals. Neurogenic pain often accompanies degenerative neurologic conditions such as MULTIPLE SCLEROSIS and pain syndromes such as trigeminal NEURALGIA and COMPLEX REGIONAL PAIN SYNDROME.

The sensation of neurogenic pain is characteristically that of a persistent tingling, burning, or "pins and needles" feeling. Some people also feel sharp stabs of pain. The diagnostic path typically includes evaluation of other potential causes for the pain in the context of any history of a musculoskeletal injury or neurologic condition. Diagnosis is often clinical (based on symptoms) after the doctor has assessed or ruled out possible conditions that could account for the symptoms.

MEDICATIONS TO TREAT NEUROGENIC PAIN

amitriptyline	baclofen
carbamazepine	dantrolene
desipramine	fluoxetine
gabapentin	paroxetine
phenytoin	sertraline
tizanidine	valproic acid

Because neurogenic pain results from NERVOUS SYSTEM dysfunction, conventional ANALGESIC MEDICATIONS such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and narcotics are not especially effective for providing pain relief. LOW-DOSE tricyclic ANTIDEPRESSANT MEDICATIONS and antiseizure medications often do provide relief, apparently through their influence on BRAIN neurotransmitters. Selective serotonin reuptake inhibitor (SSRI) antidepressants are also effective in some people. These medications may cause potentially serious side effects, especially antiseizure medications. Treatment may control pain until the underlying condition improves or may be a long-term therapeutic process, depending on the cause of the dysfunction.

See also NEURON; NEUROTRANSMITTER; NOCICEPTOR; PSYCHOGENIC PAIN.

nociceptor A specialized molecule on the dendrite of a sensory NEURON that interprets stimuli as PAIN and activates NERVE fibers (C fibers and A-delta fibers) to send pain signals to the CENTRAL NERVOUS SYSTEM. Nociceptors activate the withdrawal REFLEX—the sudden, involuntary movement to get away from the stimulus such as jerking one's hand from a hot surface. Sensory neurons often have extensive networks of dendrites, the branchlike fibers that extend from the nerve body to draw input into the neuron. Nociceptors pepper these dendrites, serving as one of the body's most primal warning mechanisms of danger from physical harm. They respond to sensations of heat, cold, sharp, and pressure.

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS), a pain relief method, uses mild electrical current to stimulate nociceptors. Researchers believe this either restores the neuron's normal perceptions of stimuli or overloads the neuron so that it cannot transmit pain signals. Doctors believe counterirritants such as capsaicin topical ointment work in a similar fashion. Some Western researchers believe ACUPUNCTURE's effectiveness for pain relief comes from its ability to stimulate or block nociceptor function; Western doctors often combine electrical stimulation with acupuncture to intensify this effect.

For further discussion of nociceptors, please see the overview section "Pain and Pain Management."

See also ALTERNATIVE METHODS FOR PAIN RELIEF; ANALGESIC MEDICATIONS; DERMATOME; PROPRIOCEPTION; SPINAL NERVES; TRADITIONAL CHINESE MEDICINE (TCM).

P

pain An unpleasant perception in response to a stimulus to the body. Multiple mechanisms contribute to the perception of pain, which follows specific and predictable pathways to the BRAIN. The brain then interprets the nature of the pain and directs the appropriate body response. Pain is one of the body's main defenses for protecting itself from harm. The pain REFLEX is the unconscious and immediate effort to remove the body part from the source of the stimulus and protect it from further damage, for example pulling the hand from contact with a sharp object and grabbing the wound (which applies pressure to stop bleeding as well as the further release of PROSTAGLANDINS and other substances that stimulate INFLAMMATION and the pain response.

Pain can take the form of many and varied characteristics: it can be sharp, dull, constant, intermittent, stabbing, throbbing, burning, localized, widespread. These characteristics help identify possible causes for the pain. The presence of health conditions such as DIABETES, PERIPHERAL VASCULAR DISEASE (PVD), MULTIPLE SCLEROSIS, and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) also provide clues as to the underlying reasons for pain.

Pain management methods target various intersections along the pain pathway. Some approaches and medications aim to reduce the production of substances (such as prostaglandins) at the site of injury, reducing the body's biochemical call to action that stimulates nociceptors. Others attempt to block NERVE signals from entering the dorsal root ganglia, and still others manipulate neurotransmitters and neuroreceptors in the brain to alter the brain's interpretation and resulting perception of pain signals that reach the thalamus and the cerebral cortex. Numerous methods are available to relieve pain, including ANALGESIC MEDICATIONS, NEURAL BLOCKADE (NERVE BLOCK), and ACUPUNCTURE.

For further discussion of pain mechanisms and pain management, please see the overview section "Pain and Pain Management."

See also ACUTE PAIN; ALTERNATIVE METHODS FOR PAIN RELIEF; CHRONIC PAIN; EUDYNIA; MALDYNIA; NEURORECEPTOR; NEUROTRANSMITTER; TERMINAL PAIN.

phantom pain The sensation of PAIN that feels as though it came from an amputated limb or other body part. Researchers believe phantom pain results from continued activity, after the AMPUTATION, among neurons in the BRAIN that interpret NERVE signals. Severed nerve fibers near the site of the amputation continue to send signals even though the surgery has removed most of their nociceptors (molecules that detect stimuli as pain). The remaining portions of the nerves continue to function, and the brain interprets their incomplete messages as pain signals. The pain often feels of the same nature as pain that might have been present in the limb before the amputation.

Many people who have phantom pain also have stump pain (pain in the remaining portion of the limb). Stump pain generally results from the damage to the nerves at the site of the amputation. Doctors do not know the extent to which stump pain contributes to phantom pain.

One therapeutic approach that may prevent phantom pain is administration of CALCITONIN, a HORMONE that prevents calcium from leaving the BONE to enter the BLOOD circulation, after the OPERATION. Doctors are uncertain why calcitonin has a preventive affect in this way. Phantom pain seems to respond better to medications used to treat NEUROGENIC PAIN than to conventional ANALGESIC MEDICATIONS. Such medications include antiseizure

medications, tricyclic ANTIDEPRESSANT MEDICATIONS, and antispasmodic medications.

See also ACUTE PAIN; CHRONIC PAIN; EUDYNIA; MALDYNIA; NEURON; NOCICEPTOR.

psychogenic pain A PAIN disorder in which the pain the person experiences has no apparent organic or physical basis. Psychogenic pain often has accompanying psychologic components such as anxiety or DEPRESSION. Recurring HEADACHE, BACK PAIN, generalized MUSCLE pain, and STOMACH pain are common presentations of psychogenic pain.

In psychogenic pain, the experience of pain is as real as if there were a clear physical cause. However, over time the nature of the pain deviates from the characteristics the doctor would expect to observe with pain of organic cause. The intensity of the pain may vary with external circumstances, for example, rather than as a result of physiologic changes that would reasonably bring about increase or decrease in pain intensity.

Psychogenic pain may be acute (come on suddenly) or chronic (persist over an extended time). Most people benefit from a combination of treatment that incorporates PSYCHOTHERAPY, nonmedication methods for pain relief, and mild ANALGESIC MEDICATIONS or other medications appropriate for the person's symptoms. Recovery depends on the ability of the person and his or her health-care team to get to the bottom of the issues presenting themselves as pain, to appropriately address and resolve them.

See also ACUTE PAIN; ALTERNATIVE METHODS OF PAIN RELIEF; BEHAVIOR MODIFICATION THERAPY; CHRONIC PAIN; GENERALIZED ANXIETY DISORDER (GAD); HYPOCHONDRIASIS; MALDYNIA; SOMATIZATION DISORDER.

T

terminal pain PAIN that results from the end-stages of disease processes such as cancer, CARDIOVASCULAR DISEASE (CVD), and AIDS. Doctors consider a health condition to be terminal when the person is likely to live less than six months. Terminal pain occurs because damage to the tissues and structures of the body is extensive and widespread. The damage often directly involves nerves. The pain may have a range of characteristics, from deep and sharp to pervasive and aching or dull.

Current standards of practice in the United States call for doctors to prescribe or health-care providers to administer ANALGESIC MEDICATIONS sufficient to relieve pain and provide comfort, even to the point of sedation if that is what is necessary. Family members may worry that such sedation is tantamount to euthanasia and hastens death, but this is not the case. The sedation, when the medication has such an effect, allows the person's body to relax more deeply. The resulting sleep increases comfort. Periods of wakefulness are then more peaceful. Administration methods such as implanted catheters and PATIENT CONTROLLED ANALGESIA (PCA) pumps allow the person to regulate the degree of pain relief.

The amounts of medications, typically NARCOTICS, necessary to accomplish this are typically much higher than conventional dosaging. Doctors who are not familiar with pain treatment or terminal illness are often concerned such amounts are too high and risk an life-threatening ADVERSE REACTION such as depressed respiration (BREATHING) and HEART RATE. However, recent studies demonstrate that terminally ill people tolerate these high doses without the adverse reactions people with less severe pain might experience. The physiologic changes that occur in the body with high or persistent levels of pain appear to block the normal processes that would result in slowed breathing. Because the body continues to adjust to balance vital functions, there is no clear OVERDOSE ceiling for narcotics taken to treat severe or terminal pain. ADDICTION, with its psychologic components, is not a concern in treatment for most severe pain, including terminal pain.

Family members who are concerned that their terminally ill loved ones are not receiving adequate pain relief should discuss this with the patient's doctors and other health-care providers and request consultation with a pain specialist if concerns continue. Medications and therapies are readily available to provide relief from terminal pain.

See also CANCER TREATMENT OPTIONS AND DECISIONS; END OF LIFE CONCERNS.

transcutaneous electrical nerve stimulation (TENS) A small device that transmits mild electrical impulses through electrodes attached to the surface of the SKIN above areas of PAIN. The impulses alter the function of the neurons (nociceptors) responsible for transmitting pain signals to the CENTRAL NERVOUS SYSTEM. TENS is primarily a treatment for CHRONIC PAIN such as neck or low BACK PAIN and is most effective for pain that is mild to moderate in severity. The doctor may suggest applying the electrodes above trigger points or major nerves, or along dermatomes, depending on the path of the pain.

Settings that provide relief are highly individualized and often TENS requires a period of trial and error before the person finds electrode positions, impulse intensity and duration, and timing settings that work. Though it is possible to set the delivery of electrical impulses at such a level as to

be painful, there is no risk for electrical shock from TENS. It is important to keep the electrode pads covered with gel. The main SIDE EFFECT with TENS is irritation to the skin from the adhesive that holds the electrodes in place or from using the electrodes without adequate gel. People who have an implanted PACEMAKER or IMPLANTABLE CARDIOVERTER DEFIBRILLATORS (ICD) cannot use TENS because the electrical current of the TENS interferes with the pacing signals.

See ACUPUNCTURE; DERMATOME; MALDYNIA; NERVE; NEURON; NOCICEPTOR; TRIGGER-POINT INJECTION.

trigger-point injection An injection of local anesthetic into an area of MUSCLE that has tightened into a knot that constricts or pressures a NERVE, causing severe PAIN. Trigger points are highly sensitive to touch or other stimuli and may form after musculoskeletal injuries and in CHRONIC PAIN conditions such as myofascial pain syndrome and FIBROMYALGIA.

Typically a pain specialist, often an orthopedic surgeon (specialist in musculoskeletal conditions) or a neurologist (specialist in conditions that affect the NERVOUS SYSTEM), administers the trigger-point injection. Depending on the cause of the damage, the injection may combine a local anesthetic with a corticosteroid medication to directly target INFLAMMATION in the area. The injection is an office procedure that causes brief discomfort from the insertion of the needle. Complete relief from pain immediately follows as the anesthetic numbs the nerves. After the numbness wears off pain relief often lasts several months and for some people is permanent.

The main risks of trigger-point injection are discomfort at the time of injection and bruising at the site that may cause superficial (surface) tenderness for several days. Ice to the site lessens the risk for bruising and relieves its discomfort. Other specific risks depend on the injection site.

See also ANESTHESIA; CORTICOSTEROID MEDICATIONS.

U–V

understanding pain Though there are numerous physiologic mechanisms responsible for PAIN, the actual experience of pain is subjective. Not only do people perceive similar pain differently but the intensity and nature of pain varies within an individual. Many people find it difficult to express to their doctors how much pain they are experiencing, or may not themselves fully understand the intensity of their pain. Pain thresholds—the levels at which pain becomes intolerable— vary widely.

The Subjective Nature of Pain

Despite all that doctors understand about the causes and mechanisms of pain, every person experiences pain differently. Numerous factors frame an individual's perceptions and experiences of pain. Key among them are

- fear about the cause of the pain
- knowledge (or lack of knowledge)
- about the mechanisms of pain
- expectations about treatments for pain
- the presence of other health conditions and their symptoms
- the appropriateness of treatment for any underlying condition that might be causing the pain
- the appropriateness of treatment for the pain, including ANALGESIC MEDICATIONS (pain relief medications)
- attitudes of others, including family members and health care providers, about the pain

Though specific kinds of pain, such as postoperative pain (pain during recovery from surgery) typically have certain characteristics, pain varies in intensity among individuals as well as in the same person.

Chronic Pain

CHRONIC PAIN is the most frustrating kind of pain because it is dysfunctional—that is, it exists without purpose—and often does not respond consistently to pain treatment approaches. The body's pain response is a protective mechanism intended to draw conscious attention to an injurious process within the body and to enforce restricted use of the affected area of the body to facilitate healing. Chronic pain exists beyond this design, often developing as an extension of purposeful pain (EUDYNIA) to become nonpurposeful (MALDYNIA) though sometimes arising for no apparent reason.

Chronic pain can be quite debilitating. Health experts estimate that more than 70 million Americans live with chronic pain that is intense enough to interfere with their participation in common functions and activities. Though movement such as walking often improves chronic pain regardless of its source, the effort of engaging in even modest physical activity can feel overwhelming.

Referred Pain

A person experiences referred pain at a location some distance from the source of the pain. The location is sometimes so far removed from the source of the pain that the person does not connect the pain with its cause. For example, gall stones in the GALLBLADDER (cholelithiasis) often cause pain in the upper back beneath the shoulder blade. Pain associated with HEART ATTACK may occur as referred pain to the left arm, shoulder, neck, and lower jaw.

Referred pain often adds challenge to diagnosing the underlying cause of the pain. Even doctors

first look for a direct cause for the pain. When one does not exist, diagnostic efforts extend to referred causes. Injured nerves are common sources of referred pain. Doctors do not fully understand the physiologic mechanisms of referred pain.

COMMON SOURCES OF REFERRED PAIN

Pain Felt	May Arise From
beneath the right shoulder	the gallbladder
in the shoulder or neck	the diaphragm or esophagus
between the shoulder blades	the stomach
in the groin	the kidneys
in the middle of the back	the kidneys or intestines
in the ear	the throat
in the lower back	the uterus or intestines
around the belly button	the appendix
beneath the sternum	the stomach or heart
in the sides (flanks)	the kidneys
under the left arm	the heart
back of the leg	the lower spine

When to Seek Medical Care for Pain

Many people wait until pain becomes unbearable before seeking medical evaluation and treatment, particularly when no other symptoms exist. Such reluctance may arise from a perception that one should be able "tough it out" or from fear that the pain indicates a serious health problem. Often pain is an early symptom, however, and prompt medical treatment can head off serious health consequences. A person should seek medical evaluation for pain that

- arises suddenly for no obvious reason
- occurs with an injury and does not improve in 48 hours
- worsens over time or recurs frequently
- is accompanied by symptoms such as blurred or double vision, numbness or loss of function in any part of the body, or difficulty breathing
- occurs in the chest, particularly as a pressing or heavy sensation
- is associated with bloody sputum, vomit, urine, or stools
- interferes with regular activities

Chest pain may indicate HEART ATTACK and requires urgent medical evaluation. All too many people wait to see whether the pain will go away instead of going to a hospital emergency room for evaluation. The time wasted on such waiting can be the difference between life and death or significant disability due to permanent heart damage. Though no one wants to feel silly for thinking he or she is having a heart attack and then discovering the problem is dyspepsia (heartburn) or acid reflux, doctors would much rather this were the case than for the person to delay seeking medical care and have the symptoms turn out to be a heart attack. Prompt medical intervention can often minimize or prevent damage to the heart.

Explaining Pain to the Doctor

Because pain is so subjective, it is often difficult to quantify its intensity when explaining it to the doctor. It can be helpful to present the doctor with the answers to questions such as these:

- Where does it hurt?
- How does the pain feel—is it sharp, dull, throbbing, steady, aching, sharp? It may be a combination of these sensations, or change in specific circumstances.
- How long has the pain been present? Has the pain changed in any way since it started?
- Under what circumstances is the pain present? Is it constant or intermittent? Does it get worse at night or with activity?
- What makes the pain worse?
- What makes the pain better?
- Does the pain limit participation in usual activities? If so, from what activities and in what ways?

Providing specific measures such as these help both the person who has pain and the doctor treating the pain to understand the effects the pain is having on the person's ability to function in daily life.

Appropriate Pain Relief

Analgesic medications (pain relief medications) are the most common therapeutic approach for acute and chronic pain. There are many kinds of medications that provide pain relief; the appropriate medications depend on the cause and nature

of the pain, other health conditions that are present, other medications the person is taking, and the person's overall health status. Nonmedication methods of pain relief, such as ACUPUNCTURE and therapeutic massage, may also be effective.

It is important to take pain relief medications according to the directions on the label for both prescription drugs and OVER-THE-COUNTER (OTC) DRUGS. Many medications prescribed for pain relief, particularly to treat postoperative pain or chronic pain, are most effective when taken on a schedule that maintains a THERAPEUTIC LEVEL of the drug in the blood circulation.

Just as people experience pain differently, people respond to pain medications differently. Consequently, the appropriate dose and schedule for the medication varies. As well, some medications are more effective for certain kinds of pain and not very effective for other kinds of pain. It is important to let the doctor know if the prescribed medication does not adequately relieve the pain or causes unpleasant side effects.

Many people, including doctors, worry about ADDICTION with the use of NARCOTICS. As a result, doctors may underprescribe or people may take less medication than is necessary to relieve the pain. However, narcotics remain the most effective analgesic medications for moderate to severe pain, especially pain during recovery from surgery or serious injuries and pain due to CANCER. Although many people do develop TOLERANCE to pain relief medications being taken over an extended time, numerous clinical studies have demonstrated that addiction very seldom occurs. Physicians who are pain management specialists or who frequently treat conditions in which pain is a key symptom are most familiar with current approaches to pain management.

See also ALTERNATIVE METHODS FOR PAIN RELIEF; DRUG INTERACTION; LIVING WITH PAIN; NEUROGENIC PAIN; PAIN MANAGEMENT IN CANCER; PATIENT-CONTROLLED ANALGESIA (PCA); PHANTOM PAIN; SCHEDULED DRUG; SIDE EFFECT; WONG-BAKER FACES PAIN RATING SCALE.

variable pain response The fluctuations that occur in the experience of PAIN. Pain's subjective nature means its intensity often varies with circumstances not directly related to the cause of the pain. Factors such as heat, cold, moisture, significant drops or rises in the barometric pressure, prolonged sitting at a computer or riding in a car, certain activities or lack of activity, the consistency with which the person takes pain relief medication, and even the foods the person consumes all may influence pain intensity. The variability of pain, especially chronic pain, is often frustrating because the person cannot always anticipate how he or she will feel, even under given circumstances. Specific conditions may act either to ease or aggravate pain, though not necessarily with predictable consistency.

See also ANALGESIC MEDICATIONS; EUDYNIA; LIVING WITH PAIN; MALDYNIA; QUALITY OF LIFE; UNDERSTANDING PAIN; WEIGHT AND PAIN.

weight and pain The influence of excessive body weight on the experience of PAIN. Excessive body weight may itself be the cause of pain, particularly pain that affects the joints, or may contribute to pain due to underlying health conditions such as FIBROMYALGIA, ANKYLOSING SPONDYLITIS, PLANTAR FASCIITIS, and GOUT. OBESITY is a risk factor for numerous chronic conditions that cause pain including OSTEOARTHRITIS and chronic BACK PAIN.

Excessive Body Weight and Musculoskeletal Structures

Excessive body weight has numerous adverse effects on the musculoskeletal system because it alters the person's posture and movement. The effects are most noticeable on the joints, which may develop chronic discomfort and aching. Every 10 pounds of body weight in excess of healthy weight increases the force the knees experience during walking by about 50 pounds each time the foot strikes the ground. Weight-bearing joints below the waist (hips, knees, ankles, and feet) are particularly vulnerable to weight-related pain. Because excessive body weight strains musculoskeletal structures, it often contributes to pain symptoms related to chronic conditions such as back pain. The pressure of the excessive weight over time may also cause damage to the joints; numerous studies implicate overweight and obesity in the development or escalated progression of osteoarthritis, the most common degenerative disorder affecting the joints.

Physical Activity and Pain Relief

Regular, moderate physical activity often improves chronic pain regardless of its source. Exercise, particularly activities that extend 20 minutes or longer, causes the body to release endorphins and other substances that act like natural pain relievers in the brain. The effects of these substances lasts far longer than the exercise session.

Regular physical exercise also strengthens muscles and connective tissues and broadens flexibility. These effects increase the stability of the joints, improving joint function. Even when pain is unrelated to the joints, these effects are beneficial for most underlying health conditions for which pain is a key symptom. And regular physical activity improves cardiovascular function, notably circulation, increasing the flow of blood to all parts of the body. Increased blood flow brings oxygen and other vital substances to areas of HEALING, helping both to speed healing and to keep scar tissue from stiffening.

However, the natural tendency is to avoid activity when pain is present. A reduced level of activity may be appropriate for certain health conditions, especially for a defined period of recovery time. Extended inactivity contributes to, rather than relieves, pain. It may also give rise to other health complications such as DEEP VEIN THROMBOSIS (DVT) or PULMONARY EMBOLISM (blood clots in the veins of the legs or in the lungs), pneumonia (fluid accumulation in the lungs, and pressure sores or decubitus ulcers. Extended inactivity also tends to encourage further weight gain, even when food intake remains the same, because reduced movement means the body uses less energy.

Appropriate Physical Activity

The doctor can recommend activities and intensity levels that are appropriate for both the health condition and the person's FITNESS LEVEL. A physical therapist or qualified fitness and training expert can develop a customized program for progressive

fitness improvement as well as weight loss. Such a consultation is especially helpful for people who have been physically inactive for a long period of time or who have challenges such as FLAT FEET or WEAK ANKLES. Moving too quickly into an intense exercise program can worsen the underlying health condition or cause other injuries. The doctor may also recommend nutritional counseling for further weight loss.

See also AEROBIC FITNESS; AEROBIC EXERCISE; DISABILITY AND EXERCISE; EXERCISE AND HEALTH; LIVING WITH PAIN; OBESITY AND HEALTH; PHYSICAL ACTIVITY RECOMMENDATIONS; WALKING FOR FITNESS; WEEKEND WARRIOR; WEIGHT AND WEIGHT MANAGEMENT.

Wong-Baker FACES pain rating scale A proprietary, commonly used visual tool designed for use with children to help them quantify the intensity of PAIN they are experiencing. Developed by Donna Wong, Ph.D., R.N. and Connie Baker, Ph.D., R.N., the FACES scale presents a sequence of six faces with expressions ranging from happy (no pain) to neutral (some pain) to sad (much pain). Children choose the face that best expresses how their pain feels to them.

Many hospitals and pediatricians use the FACES scale, available on a pocket-size card, because it is straightforward and even very young children are usually able to associate how they feel with one of the faces. The most effective approach is for the health care provider to explain to the child what the faces indicate in terms of pain severity (for example, smiling face being no pain and very sad face with tears being the worst pain) and then ask the child to choose the face that best expresses how he or she feels.

The FACES scale has associated numeric values (0 to 5) to aid the health care provider in interpreting the child's pain level. The scale also help clinicians to assess pain as a symptom during the diagnostic process as well as to evaluate the effectiveness of pain relief methods and medications for treatment of post-operative, traumatic, and chronic pain.

See also AGING, CHANGES IN PAIN PERCEPTION THAT OCCUR WITH; ANALGESIC MEDICATIONS.

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THE FACTS ON FILE ENCYCLOPEDIA OF

HEALTH AND MEDICINE

IN FOUR VOLUMES:

VOLUME 2

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An Amaranth Book

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To your health!

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The Facts On File Encyclopedia of Health and Medicine in Four Volumes: Volume 2

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VOLUME 2

FOREWORD

A big part of my role as a physician is educating my patients about their health. I take as much time as each person needs to explain prevention measures, test results, and treatment options. I encourage questions. But in the moment, sitting there in my office, most people do not yet know what to ask me. By the time questions flood their thoughts, they may be back at work or at home.

Numerous events and circumstances can challenge health, and we all need to know what actions we can take to keep ourselves healthy as well as to obtain appropriate treatment for health conditions that do affect us. Knowledge empowers all of us to make informed and appropriate decisions about health care. Certainly there is no shortage of reference material. Yet there is *so* much information available today! Even for physicians, it is challenging to keep up. How can you get to the core of what you want to know, reliably and to the level of detail you need?

The Facts On File Encyclopedia of Health and Medicine is a great resource for up-to-date health information presented in a manner that is both comprehensive and easy to understand no matter what your level of medical knowledge. The encyclopedia organizes entries by body system. The progression of body systems—and entries—throughout the encyclopedia presents topics the way you think about them.

Going beyond this basic structure, however, is another layer of organization that particularly appeals to me, which is a comprehensive structure of cross references that integrates entries across body systems. After all, your body functions in an integrated way; so, too, should a reference series that discusses your body's health. Not very much that happens with your health affects one part of your body in isolation from other body structures and functions. Your body attempts to compensate and adjust, often without your awareness, until it can no longer accommodate the injury or illness. The symptoms you bring to your doctor may reflect this compensation, for example frequent headaches that point not to brain tumor (as many people fear but is very rare) but to eye strain or muscle tension or sometimes to hypertension (high blood pressure).

In my medical practice I emphasize integrative health care, embracing the philosophy that health exists as the intricate intertwining of the body's many systems, structures, and functions. So, too, does the care of health. I received my medical degree from Tufts University School of Medicine in Boston, an institution noted for remaining at the forefront of the medical profession. I also completed clinical programs in Mind-Body Medicine at Harvard University, Integrative Medicine at the University of Arizona School of Medicine, and Medical Acupuncture at the University of California-Los Angeles (UCLA). I am a board-certified obstetrician-gynecologist, a board-certified clinical nutritionist, and a licensed acupuncturist. I see patients in my practice in Cincinnati, Ohio; I teach, I lecture, and I frequently go on television and radio to talk about health topics. In each of these areas, I encourage people to think about their health and health concerns from an integrative perspective. When you understand your health from multiple dimensions, you can better understand what to do to keep yourself as healthy as possible.

I wish you the best of health for all of a long, satisfying life. But when the time comes that you must make decisions about medical care, I want you to have the knowledge to make informed

choices that are right for you. Whether you start here and move on to more specialized resources or locate all the information you need within these four volumes, you will find *The Facts On File Encyclopedia of Health and Medicine* to be a most valuable reference resource.

—Maureen M. Pelletier, M.D., C.C.N., F.A.C.O.G.

HOW TO USE
THE FACTS ON FILE ENCYCLOPEDIA OF HEALTH AND MEDICINE

Welcome to *The Facts On File Encyclopedia of Health and Medicine*, a four-volume reference set. This comprehensive resource is an indispensable reference for students, allied health professionals, physicians, caregivers, lay researchers, and people seeking information about health circumstances and conditions for themselves or others. Entries present the latest health concepts and medical knowledge in a clear, concise format. Readers may easily accumulate information and build a complete medical profile on just about any health or medical topic of interest or concern.

A New Paradigm for the Health and Medical Encyclopedia

As the art and science of health and medicine continues to evolve, with complex and elegant discoveries and new techniques, medications, and treatments emerging all the time, the need has arisen for a new paradigm for the encyclopedia of health and medicine—a rethinking of the old, and increasingly outmoded, presentations. Carefully researched and compiled, *The Facts On File Encyclopedia of Health and Medicine* offers many distinguishing features that present readers and researchers with an organization as up-to-date and compelling as the breakthrough information its entries contain.

Recognizing the current emphasis on presenting a truly integrative approach to both health and disease, *The Facts On File Encyclopedia of Health and Medicine* organizes content across volumes within a distinctive format that groups related entries by body system (for example, "The Cardiovascular System") or by general health topic (for example, "Genetics and Molecular Medicine"):

- **Volume 1** presents the sensory and structural body systems that allow the body to engage with its surroundings and the external environment.
- **Volume 2** presents the cell- and fluid-based body systems that transport nutrients, remove molecular wastes, and provide protection from infection.
- **Volume 3** presents the biochemical body systems that support cellular functions.
- **Volume 4** presents topics that apply across body systems (such as "Fitness: Exercise and Health") or that address broad areas within health care (such as "Preventive Medicine").
- The appendixes provide supportive or additional reference information (such as "Appendix X: Immunization and Routine Examination Schedules").

Following Research Pathways

The Facts On File Encyclopedia of Health and Medicine's organization and structure support the reader's and researcher's ease of use. Many encyclopedia users will find all the information they desire within one volume. Others may use several or all four of the encyclopedia's volumes to arrive at a comprehensive, multifaceted, in-depth understanding of related health and medical concepts and information. Researchers efficiently look up information in *The Facts On File Encyclopedia of Health and Medicine* in several ways.

Each section's entries appear in alphabetical order (except the entries in Volume 4's "Emergency and First Aid" section, which are grouped by type of emergency). The researcher finds a desired entry by looking in the relevant volume and section. For example, the entry for **acne** is in Volume 1 in the section "The Integumentary System" and the entry for **stomach** is in Volume 3 in

the section "The Gastrointestinal System." The researcher can also consult the index at the back of the volume to locate the entry, then turn to the appropriate page in the volume.

Terms that appear in SMALL CAPS within the text of an entry are themselves entries elsewhere in *The Facts On File Encyclopedia of Health and Medicine*. Encyclopedia users can look up the entries for those terms as well, for further information of potential interest. Such SMALL CAPS cross references typically provide related content that expands upon the primary topic, sometimes leading the user in new research directions he or she might otherwise not have explored.

For example, the entry **hypertension** is in the section "The Cardiovascular System." The entry presents a comprehensive discussion of the health condition hypertension (high blood pressure), covering symptoms, diagnosis, treatment options, risk factors, and prevention efforts. Among the numerous SMALL CAPS cross references within the hypertension entry are the entries for

- **retinopathy**, an entry in the section "The Eyes" in Volume 1, which discusses damage to the eye that may result from untreated or poorly managed hypertension
- **blood pressure**, an entry in the Volume 2 section "The Cardiovascular System," which discusses the body's mechanisms for maintaining appropriate pressure within the circulatory system
- **stroke** and **heart attack**, entries in Volume 2's "The Cardiovascular System" about significant health conditions that may result from hypertension
- **kidney,** an entry in the section "The Urinary System" in Volume 3, which discusses the kidney's role in regulating the body's electrolyte balances and fluid volume to control blood pressure
- **atherosclerosis, diabetes, hyperlipidemia,** and **obesity**, entries in the sections "The Cardiovascular System" in Volume 2, "The Endocrine System" in Volume 3, and "Lifestyle Variables: Smoking and Obesity" in Volume 4, and all of which are health conditions that contribute to hypertension

Following the path of an encyclopedic entry's internal cross references, as shown above, can illuminate connections between body systems; define and apply medical terminology; reveal a broad matrix of related health conditions, issues, and concerns; and more. The SMALL CAPS cross references indicated within the text of encyclopedic entries lead encyclopedia users on wide-ranging research pathways that branch and blossom.

At the end of the entry for **hypertension** a list of cross references gathered in alphabetical order links together groups of related entries in other sections and volumes, such as **smoking cessation** in Volume 4's "Lifestyle Variables: Smoking and Obesity," to provide specific, highly relevant research strings. These *see also* cross references also appear in SMALL CAPS, identifying them at a glance. Encyclopedia users are encouraged to look here for leads on honing research with precision to a direct pathway of connected entries.

So, extensive cross-references in *The Facts On File Encyclopedia of Health and Medicine* link related topics within and across sections and volumes, in both broad and narrow research pathways. This approach encourages researchers to investigate beyond the conventional level and focus of information, providing logical direction to relevant subjects. Each cross-referenced entry correspondingly has its own set of cross references, ever widening the web of knowledge.

Using the Facts On File Encyclopedia of Health and Medicine

Each section of the encyclopedia begins with an overview that introduces the section and its key concepts, connecting information to present a comprehensive view of the relevant system of the human body or health and medical subject area. For most body systems, this overview begins with a list and drawings of the system's structures and incorporates discussion of historic, current, and future contexts.

Entries present a spectrum of information from lifestyle factors and complementary methods to the most current technologic advances and approaches, as appropriate. Text that is set apart or bold within an entry gives an important health warning, or targets salient points of interest to add layers of meaning and context. Lists and tables

collect concise presentations of related information for easy reference.

Each type of entry (mid-length and longer) incorporates consistent elements, identified by standardized subheadings:

- ***Entries for health conditions and diseases*** begin with a general discussion of the condition and its known or possible causes and then incorporate content under the subheadings "Symptoms and Diagnostic Path," "Treatment Options and Outlook," and "Risk Factors and Preventive Measures."
- ***Entries for surgery operations*** begin with a general discussion of the procedure and then incorporate content under the subheadings "Surgical Procedure," "Risks and Complications," and "Outlook and Lifestyle Modifications."
- ***Entries for medication classifications*** begin with a general discussion of the type of medication and its common uses and then incorporate content under the subheadings "How These Medications Work," "Therapeutic Applications," and "Risks and Side Effects."
- ***Entries for diagnostic procedures*** begin with a general discussion of the test or procedure and then incorporate content under the subheadings "Reasons for Doing This Test," "Preparation, Procedure, and Recovery," and "Risks and Complications."

Entries in Volume 4's section "Emergency and First Aid" are unique within the orientation of *The Facts On File Encyclopedia of Health and Medicine* in that they feature instructional rather than informational content. **These entries do *not* replace appropriate training in emergency response and first aid methods.** Rather, these entries provide brief directives that are appropriate for guiding the actions of a person with little or no first aid training who is first on the scene of an emergency.

Each volume concludes with a complete, full index for the sections and entries within the volume. Volume 4 of *The Facts On File Encyclopedia of Medicine* contains a comprehensive index for all four encyclopedia volumes that researchers can use to quickly and easily determine which volumes contain desired sections or entries.

The Facts On File Encyclopedia of Health and Medicine in Four Volumes

PREFACE TO VOLUME 2

Volume 2 of the four-volume *The Facts On File Encyclopedia of Health and Medicine* presents the body systems that nourish, cleanse, and protect the body. These are the systems of cells and fluids and the structures that transport them throughout the body. Though distinct in their functions and purposes, these systems overlap and integrate with one another in inseparable ways.

The Cardiovascular System

Volume 2 opens with "The Cardiovascular System," the structures and functions that carry blood throughout the body. An amazing pump—the heart—and miles of blood vessels—the arteries and veins—are the hallmarks of this system that mostly functions without conscious awareness save for the regular rhythm of the heartbeat.

Advances in medical technology make it possible to treat cardiovascular disease that even 30 years ago would have been fatal. Medications and devices can regulate the functions of the heart to overcome or compensate for disease and damage. Heart transplantation and mechanical heart substitutes, once the dream of surgeons but the venue of fiction, are now among the standard treatment options for some heart conditions. Many of the entries in "The Cardiovascular System" discuss these sophisticated therapeutic approaches. Yet lifestyle strongly influences cardiovascular health, which encyclopedia users will detect as a prevalent theme in this section.

The Blood and Lymph

These two fluid-based systems of the blood and the lymph have separate yet interconnected circulatory networks. The blood bridges the functions of the cardiovascular and pulmonary systems, circulating through arteries, veins, and capillaries to carry oxygen and nutrients to, and metabolic wastes from, cells throughout the body. The cells that do this work, the erythrocytes, make up about half the blood's cells and give blood its characteristic red color. The lymph network is the immune system's major highway; its cells are lymphocytes. These white blood cells lack color, giving lymph the appearance of watery milk. Lymph circulates through its own structure of lymph vessels though crosses from the lymphatic circulation to the blood circulation at two junctions, the cisterna chyli and the thoracic duct.

The Pulmonary System

The pulmonary system is the body's primary interaction with the external atmosphere. The lungs pull oxygen-bearing air deep into the body where an intricate molecular exchange takes place to load each outgoing breath with metabolic waste. The laws of physics—particularly those relating to relationships between pressure and volume, regulate the functions of the pulmonary system. The pulmonary system intimately interacts with the blood and the cardiovascular system. Without these interactions, the functions of the pulmonary system are of little value to the body. Acquired pulmonary disease often coexists with cardiovascular disease; entries in this section provide both discussion and cross-references to establish such connections.

The Immune System and Allergies

The immune system is a complex network of primarily cells and substances that circulate in the lymph and the blood and reside in the tissues. With much current research focused on HIV/AIDS and the understanding and treatment of cancer, knowledge of the immune system's functions con-

tinues to evolve at a pace not experienced since the discovery of antibiotics and vaccines. New approaches to conditions across the spectrum of health incorporate methods that use the immune system's own mechanisms to prevent and fight infection and disease.

Infectious Diseases

Infectious diseases remain a significant threat to health throughout the world. Vaccines, antibiotics, antiviral medications, and other therapies in combination with community health practices such as sanitation measures and water purity standards now can prevent or treat many infections that were fatal not so long ago. Entries in this section integrate medical treatments and lifestyle or preventive approaches, as both are essential to control the health consequences of infectious diseases.

Cancer

Cancer is a broad category of disease that can affect any body system. Current medical thinking is that cancer represents an intersection of genetic, immune, and lifestyle factors in varying mixes depending on the type of cancer. Like in the immune system, knowledge in this area is rapidly and continually changing. New treatments take advantage of new understandings. The entries in this section, "Cancer," cover topics that apply to cancer in general. Encyclopedia users will find entries for specific types of cancer in the relevant body system sections.

THE FACTS ON FILE ENCYCLOPEDIA OF

HEALTH AND MEDICINE

IN FOUR VOLUMES:

VOLUME 2

THE CARDIOVASCULAR SYSTEM

The cardiovascular system circulates BLOOD through the body to deliver nutrients and collect wastes from cells. Physician specialists who treat conditions of the HEART and blood vessels are cardiologists. This section, "The Cardiovascular System," presents an overview of the structures and functions of the cardiovascular system, a discussion of cardiovascular health and disorders, and entries about the health conditions that can affect the cardiovascular system.

Structures of the Cardiovascular System

HEART
- PERICARDIUM
- CORONARY ARTERIES
- MYOCARDIUM
- ENDOCARDIUM
- superior VENA CAVA
- inferior vena cava
- right atrium
- tricuspid valve
- right ventricle
- pulmonary valve
- right pulmonary ARTERY
- left pulmonary artery
- left atrium
- mitral valve
- left ventricle
- aortic valve
- AORTA
- SEPTUM
- SINOATRIAL (SA) NODE
- BUNDLE OF HIS
- left BUNDLE BRANCH
- right bundle branch
- Purkinje fibers
- ATRIOVENTRICULAR (AV) NODE

arteries of the head and neck
- occipital
- temporal
- CIRCLE OF WILLIS
- facial
- maxillary
- carotid

arteries of the upper torso and extremities
- brachiocephalic
- right subclavian
- left subclavian
- axillary
- brachial
- radial
- ulnar
- palmar arch

arteries of the trunk
- abdominal aorta
- intercostal
- celiac
- gastric
- hepatic
- splenic
- superior mesenteric
- inferior mesenteric
- renal

arteries of the lower torso and extremities
- common iliac
- external iliac
- internal iliac
- femoral
- deep femoral
- popliteal
- anterior tibial
- posterior tibial
- dorsal arch

veins of the head and neck
- superior sagittal sinus
- inferior sagittal sinus
- transverse sinus
- anterior facial
- external jugular
- internal jugular

veins of the upper torso and extremities
- brachiocephalic
- subclavian
- axillary
- brachial
- cephalic
- basilic

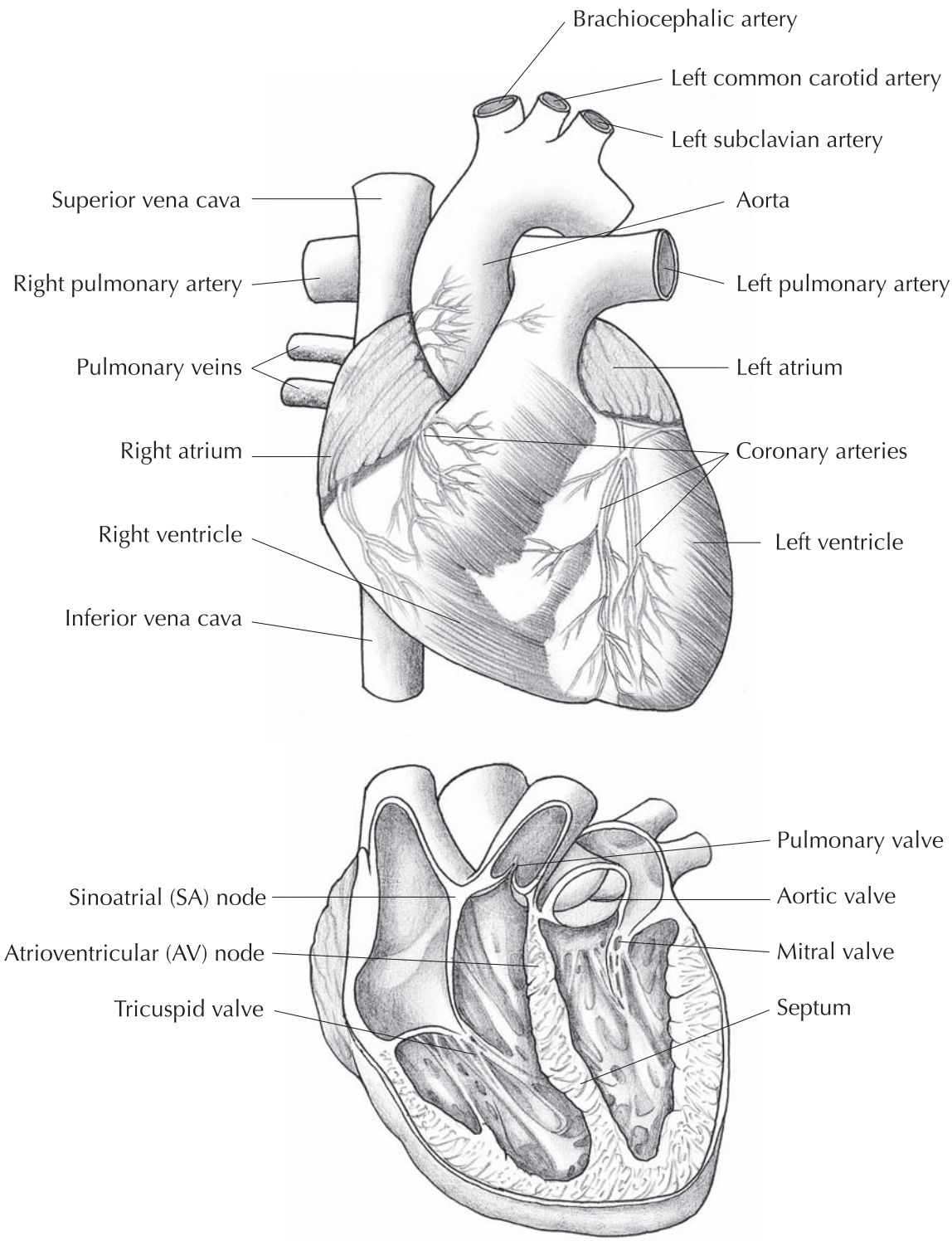
veins of the trunk
- splenic
- portal
- renal
- superior mesenteric
- inferior mesenteric
- external iliac
- internal iliac

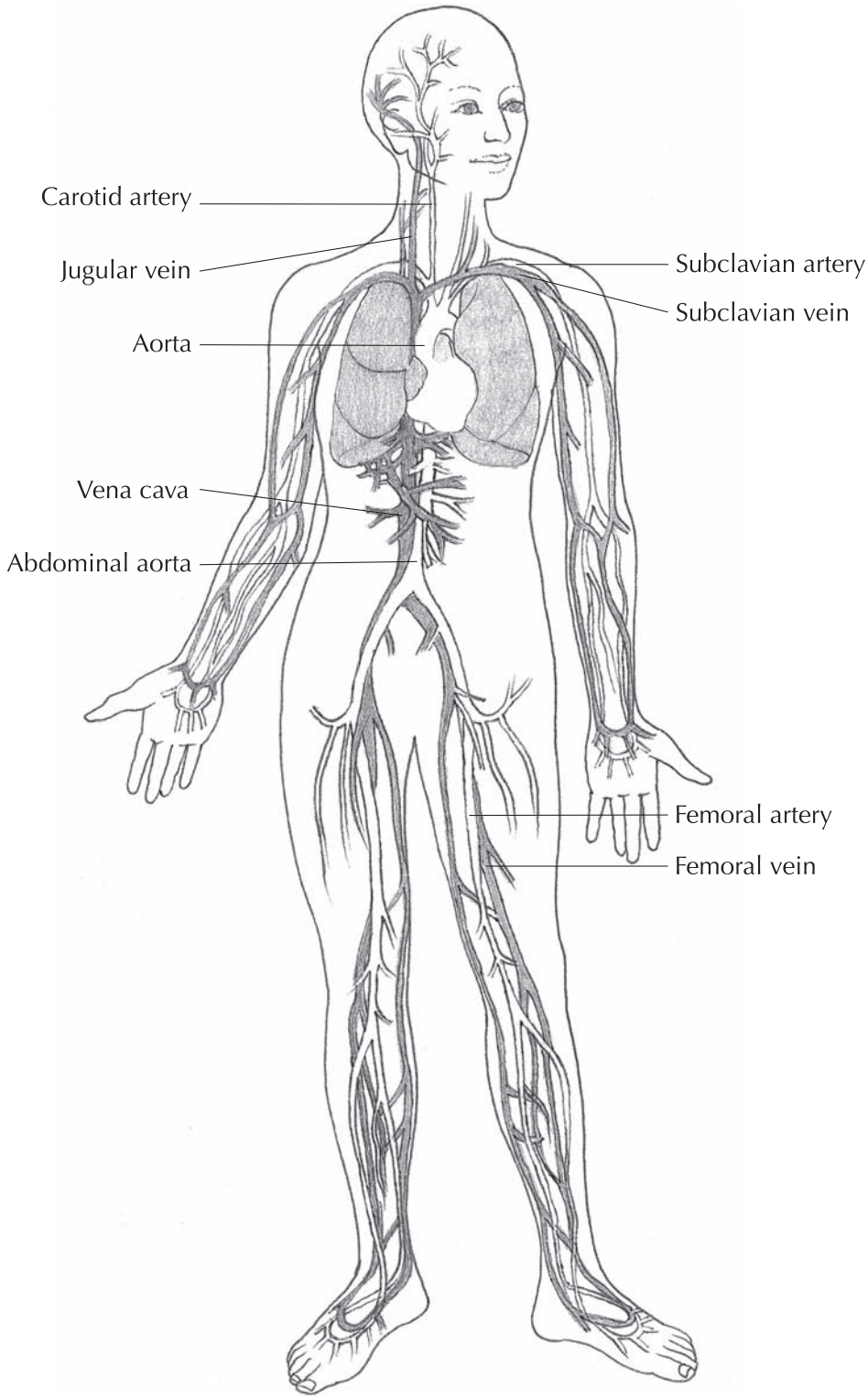
veins of the lower torso and extremities
- femoral
- popliteal
- anterior tibial
- posterior tibial
- great saphenous
- small saphenous
- dorsal arch

Functions of the Cardiovascular System

The cardiovascular system circulates blood through the body to supply cells with nutrients, notably oxygen and GLUCOSE, and to remove the waste byproducts of METABOLISM. The centerpiece of this system is the heart, a muscular organ about the size and shape of a closed fist that beats 70 to 90 times a minute in a healthy adult at rest. The body's circulation is a closed, pressurized system that contains a constant blood volume of about 10 liters (2.6 gallons). An extensive network of blood vessels–which, if stretched end to end, would traverse 100,000 miles—transports that blood through the body.

Cardiovascular function defines life and death. The cardiovascular system is among the first of


Brachiocephalic artery
Left common carotid artery
Left subclavian artery
Superior vena cava
Aorta
Right pulmonary artery
Left pulmonary artery
Pulmonary veins
Left atrium
Right atrium
Coronary arteries
Right ventricle
Left ventricle
Inferior vena cava
Pulmonary valve
Sinoatrial (SA) node
Aortic valve
Atrioventricular (AV) node
Mitral valve
Tricuspid valve
Septum


Carotid artery
Jugular vein
Aorta
Vena cava
Abdominal aorta
Subclavian artery
Subclavian vein
Femoral artery
Femoral vein

the body systems to become functional. The rudimentary heart begins beating at three weeks gestational age, and by eight weeks the heart's formation is complete. Doppler ULTRASOUND, a noninvasive procedure that uses sound waves to detect motion, can detect the fetal heartbeat at 10 to 12 weeks into PREGNANCY.

PULSE and BLOOD PRESSURE—the rate and force of blood as it flows through the arteries—are among the basic vital signs health-care providers assess to determine core health status and indeed life or death. When the heart stops beating, pulse and blood pressure cease. Cells in the BRAIN and the MYOCARDIUM, deprived of oxygen, begin to die. Though myocardial cells are capable, to an extent, of regenerating, brain cells are not. Only two to three minutes without oxygen can result in permanent neurologic damage and even death.

The heart The heart lies behind the protective enclosure of the rib cage, its left side beneath the STERNUM (breastbone) and its right side extending about to the center of the right BREAST. A tough sac, the PERICARDIUM, encases the heart. A thin layer of fluid between the pericardium and the myocardium (heart MUSCLE) allows the heart to move continuously without friction in much the same way motor oil permits pistons to glide freely within an engine. A crownlike network of arteries, the CORONARY ARTERIES, encircles the outer surface of the myocardium. This network directs roughly 20 percent of the body's blood supply and 70 percent of the blood's oxygen content to the heart with each heartbeat. A thin membrane, the ENDOCARDIUM, lines the chambers of the heart. The endocardium is so smooth not even platelets, the blood's clotting cells, can stick to it.

The heart's four chambers collect and expel blood through rhythmic, synchronized contractions. The two upper chambers, the atria, receive blood into the heart. The two lower chambers, the ventricles, pump blood from the heart. One-way valves regulate the flow and volume of blood into and out of each chamber. The four chambers of the heart contract and relax in precise coordination. The walls of the heart become progressively thicker from the atria to the ventricles, reaching their greatest density and STRENGTH in the left ventricle to support its work to contract with enough force to pump blood to the most distant cells in the body. A thick inner wall, the septum, separates the heart's chambers.

A cluster of specialized NERVE cells, the SINOATRIAL (SA) NODE, generates a "pacing" electrical impulse that starts with the right atrium and builds momentum as it courses through the cells and fibers of the myocardium. Other electrical structures—the BUNDLE OF HIS, right BUNDLE BRANCH and left bundle branch, ATRIOVENTRICULAR (AV) NODE, and the Purkinje fibers—amplify and focus the electrical impulses so they reach maximum intensity when they arrive at the left ventricle. This collective effort forms the CARDIAC CYCLE, the sequential and coordinated contraction and relaxation of the atria and the ventricles.

The right atrium and right ventricle, known collectively as the right heart, handle deoxygenated blood returning from the body. Blood flows from the superior VENA CAVA (bringing blood from the upper body) and inferior vena cava (bringing blood from the lower body) into the right atrium, which pumps it through the tricuspid valve into the right ventricle. The right ventricle pumps the blood through the pulmonary valve into the pulmonary ARTERY, which carries it to the LUNGS for OXYGENATION.

The left atrium and left ventricle, known collectively as the left heart, handle oxygenated blood. The PULMONARY VEINS (right and left, from the right lung and left lung respectively) deliver oxygenated blood from the lungs to the left atrium. The left atrium pumps the blood through the mitral valve into the left ventricle. The left ventricle propels blood through the aortic valve into the AORTA, the body's largest blood vessel, and on its circulatory journey.

The blood vessels Blood vessels circulate blood throughout the body. Arteries carry blood *from* the heart. All arteries except the pulmonary artery carry oxygenated blood; the pulmonary artery carries deoxygenated blood from the heart to the lungs. Arteries have multilayered, muscular walls that pulsate in coordination with the heart's contractions. The innermost layer, the intima, functions in the same fashion as the endocardium to keep the blood from sticking to the artery's inner walls. Veins carry blood *to* the heart. All veins except the two pulmonary veins carry deoxygenated blood; the pulmonary veins transport

oxygenated blood to the heart from the lungs. Veins have thin, flexible walls with valves that allow blood to flow only in one direction.

The smallest of the blood vessels, the arterioles and the venules, have walls fractions of a millimeter in thickness and so narrow that only the smallest of blood cells, oxygen-bearing erythrocytes, can squeeze through and even they must pass single-file. These tiny vessels mesh into the CAPILLARY BEDS, the terminus for the blood's journey. Blood cells are at their busiest here, exchanging oxygen and other nutrients for carbon dioxide and other metabolic wastes.

Most blood vessels exist in mirror structures on each side of the body and occur in parallel. The femoral artery and femoral VEIN run together, for example, one set serving each upper leg. Often these vessels have similar names, such as the femorals or the popliteal artery and popliteal vein. As the coronary arteries channel oxygenated blood to the heart, the arteries that form the CIRCLE OF WILLIS at the base of the brain direct oxygen-rich blood to the brain.

The circulation Each beat of the heart propels 80 milliliters (2.5 ounces) of blood into the AORTA, the largest artery in the body. It takes about 20 seconds for that same volume of blood to complete its journey through the body's blood vessels and return to the heart. Every minute, 5 to 6 liters (0.85 to 1.5 gallons) of blood circulates through the body—the equivalent of three 2-liter bottles of soda. In the course of a day the volume of blood the heart pumps is enough to fill an Olympic-size swimming pool.

Pressure aids the heart in pushing blood through the blood vessels. A complex interaction of hormones and other chemicals regulates blood pressure. Blood in the arteries is under high pressure, helping push it to the cells that require the oxygen and nutrients it carries. The pressure within the arteries allows blood to defy the pull of gravity as it courses to the body's tissues. Because the circulation is a closed system, the pressure of the arterial flow helps send blood through the veins as well, much as the pressure of a river's water continues to create current in the small streams that branch from it. The pressure of the blood within veins is significantly lower than the pressure within arteries. Valves in the veins act as one-way gates to keep blood flowing back to the heart. Skeletal muscles encase the major veins, further supporting them. With every movement these muscles massage the veins to help move returning blood along its passage back to the heart.

Health and Disorders of the Cardiovascular System

The cardiovascular system has the capacity to maintain healthy function in adults well into the seventh decade and beyond, though for many people it does not. More than 70 million Americans are LIVING WITH CARDIOVASCULAR DISEASE; 10 million of them are disabled to an extent that they are unable to enjoy the lifestyles they desire as a result. CARDIOVASCULAR DISEASE (CVD)—a collective term for the many health conditions that affect the heart and blood vessels—causes the deaths of more than 900,000 Americans each year, making it the leading cause of death among men and women alike in the United States. Most CVD among Americans is acquired, developing through the course of life and nearly always as a consequence of lifestyle factors. Genetic factors and other health conditions, notably DIABETES, may also contribute.

FORMS OF CARDIOVASCULAR DISEASE (CVD)

ANEURYSM	ARRHYTHMIA
ATHEROSCLEROSIS	BUNDLE BRANCH BLOCK
CARDIOMYOPATHY	CONGENITAL HEART DISEASE
CORONARY ARTERY DISEASE (CAD)	DEEP VEIN THROMBOSIS (DVT)
ENDOCARDITIS	HEART FAILURE
HYPERLIPIDEMIA	HYPERTENSION (high BLOOD PRESSURE)
HYPOTENSION (low blood pressure)	INTERMITTENT CLAUDICATION
ISCHEMIC HEART DISEASE (IHD)	KAWASAKI'S DISEASE
LONG QT SYNDROME (LQTS)	MYOCARDITIS
PERICARDITIS	PERIPHERAL VASCULAR DISEASE (PVD)
PRIMARY PULMONARY HYPERTENSION	RAYNAUD'S SYNDROME
RHEUMATIC HEART DISEASE	SICK SINUS SYNDROME
STROKE	TRANSIENT ISCHEMIC ATTACK (TIA)
VALVULAR HEART DISEASE	WOLFF-PARKINSON-WHITE SYNDROME

About 30,000 infants are born with CONGENITAL HEART DISEASE—defects of the heart and blood vessels—each year. Heart defects are the most com-

mon birth defects in the United States. Some congenital heart defects are life-threatening, such as tetralogy of Fallot and transposition of the great arteries (TGA), and require extensive surgical reconstruction or HEART TRANSPLANTATION for the infant to survive. Many congenital heart anomalies are correctable with surgery or treatable with medications, allowing the child relatively normal life experiences and life expectancy. Researchers do not know the causes of many of these defects, which arise early in embryonic development.

Though some of the most exciting technological advances in modern medicine are those that improve treatment for cardiovascular conditions such as heart failure, health experts believe lifestyle measures could prevent as much as 90 percent of acquired cardiovascular disease. Cardiovascular health depends on four key lifestyle factors:

- not smoking
- nutritious eating habits
- daily physical exercise
- maintaining healthy weight

These factors maintain the cardiovascular system in optimal health. Yet despite the overwhelming evidence that these factors do in fact prevent cardiovascular disease, two thirds of the US population is overweight and three fourths do not get the minimum recommended physical exercise. Two lifestyle-related health conditions that strongly influence cardiovascular disease are diabetes and OBESITY. Type 2 diabetes, the most common form of diabetes among American adults, and obesity are closely linked. When these two conditions coexist, some form of cardiovascular disease is almost certainly present as well.

Traditions in Medical History

The heart mystified ancient physicians. Though all cultures recognized the relationship between the heart and life itself, they differed vastly in their interpretations of what that relationship was. The Egyptians held the heart to be the base of intellect and emotion in life and the measure of that life's worth upon a person's passage to the afterworld. Mesopotamian and Sumerian physicians used MEDICINAL HERBS AND BOTANICALS to treat ailments such as pounding of the pulse and heart weakness—perhaps references to conditions contemporary doctors might diagnose as PALPITATIONS and HEART FAILURE.

Ancient Chinese physicians speculated that the heart circulated all of the body's vital substances, including air, through a complex network of vessels and passageways. Within the tenets of primitive Chinese medicine the pulse spoke to the physician, its rhythms and patterns presenting the story of the body's health and illnesses. A gifted physician could interpret hundreds of details from numerous pulse points. Intricate readings of the pulse remain integral to TRADITIONAL CHINESE MEDICINE (TCM) as practiced today.

In Western medicine, Greek and Roman physicians of antiquity postulated that the LIVER produced the body's supply of blood from the food a person ate. The veins carried the blood from the liver to the other organs, which consumed it. The arteries, in this scheme, arose from the heart though carried air. The role of the heart itself was somewhat ambiguous, with some physicians believing the heart pulled air into the arteries through pores in the skin and others that it had nothing to do with any sort of circulation but instead gave rise to emotions and thoughts.

The Greek physician GALEN (130–200) both consolidated and expanded the understandings of human anatomy and physiology of his time into the principles and practices that became the foundation of Western medicine for the ensuing 1,200 years. In Galen's view, the veins delivered to the heart blood the liver made, and the arteries carried the air drawn into the body through pores in the skin. Other pores between the chambers of the heart, according to Galen, mixed the blood and the air. Each beat of the heart then propelled this mixture through the arteries to the organs of the body. Though this schematic makes little sense in the context of current knowledge, despite its fundamental inaccuracies it came fairly on target in its projections of the body's need for oxygen and the role of the cardiovascular system to deliver it. In Galen's day, the concept was the ideal blend of the many understandings and misunderstandings about the functions of the body.

FIRST DISCOVERY OF CIRCULATION

Records survive that document the accurate perception by Arabic physician Ibn al-Nafis in 1242 of the heart's chambers and of the closed circulation of the blood. The discovery did not reach other parts of the world, however, and came to light only in the 1920s when a medical scholar uncovered an-Nafis's medical writings and drawings.

Galenism defined medical knowledge and practice into the 17th century. In 1628 English physician William Harvey (1578–1657) published the document that would become the turning point of modern Western medicine: *Exercitatio Anatomica De Motu Cordis et Sanguinis in Animalisbus*, or in English, *An Anatomical Treatise on the Motion of the Heart and Blood in Animals*. Harvey deduced, correctly, that the heart pumped the same blood repeatedly in a closed circuit through the body, with the arteries carrying oxygenated, bright blood from the heart and the veins returning deoxygenated, dark blood to the heart. *De Motu Cordis* established the basis of cardiovascular structure and function that still frames understanding of the heart's mechanical operation.

Breakthrough Research and Treatment Advances

The most significant breakthrough in cardiology was the development of the CARDIOPULMONARY BYPASS machine, successfully used for the first time in the 1950s and the cornerstone of cardiovascular surgery today. Cardiopulmonary bypass makes it possible for the cardiovascular surgeon to stop the heart, yet maintain the body's blood circulation and oxygenation. Advances in surgery techniques, technology, and pharmacology in the last decade of the 20th century made reconstructive operations for congenital heart malformations, CORONARY ARTERY BYPASS GRAFT (CABG), and even HEART TRANSPLANTATION routine offerings on the slate of treatment options. Countless people can enjoy extended, productive lives as a result.

The limited supply of donor hearts for transplantation has focused much technology research on development of a feasible artificial replacement heart that could be fully contained within the chest. In 2001 cardiovascular surgeons implanted the first of the new generation of total artificial hearts in a handful of people suffering from end-stage cardiovascular disease. Other researchers looked toward assisting, rather than replacing, ailing hearts, resulting in implanted VENTRICULAR ASSIST DEVICES (VADS) that function in coordination with the native heart. Some cardiovascular surgeons see VADs as bridge devices to sustain cardiovascular function while awaiting a donor heart for transplantation, and others as an end-stage treatment for people who have complete HEART FAILURE but are not candidates for heart transplantation because of age or other health conditions. Now an approved treatment option for end-stage heart failure, the VAD can stay in place for as long as needed.

Cardiovascular surgeons continue to explore ways to incorporate microsurgery techniques in operations such as CABG, looking to reduce the trauma of entering the chest cavity to fully expose the heart. Minimally invasive endoscopic procedures already permit operations on arteries and veins, as well as for CABG when only one coronary artery needs replacement. Cardiovascular surgeons also are beginning to apply minimally invasive techniques for valve repair and other operations on the heart.

Breakthroughs in genetics show great promise for both treatment and prevention of cardiovascular conditions in the decades ahead. Researchers have identified numerous genes responsible for heart conditions such as LONG QT SYNDROME (LQTS), certain forms of CARDIOMYOPATHY, ATHEROSCLEROSIS, and some forms of heart failure. Many of these genes interact with environmental factors such as diet and level of physical activity, contributing to rather than outright causing heart disease. Researchers are exploring ways to use GENE THERAPY to inactivate destructive genetic influences and enhance genetic influences that support or improve cardiovascular function. These influences likely explain why some people get cardiovascular diseases and others do not even when their lifestyles are similar.

Researchers also continue to unravel the mysteries of metabolism, gaining increased understanding of how exercise and nutrition affect cell function and how processes such as atherosclero-

sis get started in the body. One focus of such research is on INSULIN, which has numerous roles in the body beyond regulating glucose balance. Insulin appears to be a key factor in many functions related to cardiovascular health and disease, including cholesterol metabolism and cell activity.

Cardiology in the coming decades promises to be an intriguing blend of high-tech solutions and simple lifestyle methods. With other advances in medicine eliminating many of the circumstances that have historically resulted in early death, such as INFECTION, today's generations may be the first to fully experience the capacity of the cardiovascular system to sustain life well into the eighth decade and beyond, pushing LIFE EXPECTANCY as well as QUALITY OF LIFE to new levels.

A

aerobic fitness The efficiency with which the cardiovascular system functions to meet the oxygen needs of cells throughout the body, particularly under the increased pressure of intense physical activity or exercise. The higher a person's aerobic FITNESS LEVEL, the more air the LUNGS can take in each breath, the more oxygen that enters the BLOOD, and the more blood the HEART can eject with each contraction. The outcome is that the cardiovascular system can deliver higher concentrations of oxygen to body tissues with less effort, which increases ENDURANCE. Aerobic fitness is a key measure of cardiovascular health.

ACTIVITIES THAT IMPROVE AEROBIC FITNESS

aerobic dance	basketball	bicycling
canoeing	cross-country skiing	handball
hiking	ice skating	jogging
kayaking	racquetball	roller skating
rowing	running	shooting hoops
snowshoeing	soccer	spinning
squash	stair climbing	stationary cycling
step aerobics	swimming	tennis
treadmill	volleyball	walking

Physical activities that exercise the muscles to a level that increases the HEART RATE and BREATHING rate for a sustained time of 15 minutes or longer provide an aerobic workout for the body that strengthens cardiovascular efficiency and improves aerobic fitness. Consistency is the key to aerobic fitness. Health experts recommend aerobic activity three to four times a week, ideally in sessions that are 30 to 45 minutes long. The higher a person's aerobic fitness level, the easier it is to sustain aerobic activity for longer periods of time.

See also AEROBIC CAPACITY; AEROBIC EXERCISE; AGING, CARDIOVASCULAR CHANGES THAT OCCUR WITH; CONDITIONING; EXERCISE AND HEALTH; LIFESTYLE AND HEALTH; MUSCLE; PHYSICAL ACTIVITY RECOMMENDATIONS; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; WALKING FOR FITNESS.

aging, cardiovascular changes that occur with The most significant age-related changes in cardiovascular function occur at birth in both sexes and with MENOPAUSE in women. Though changes in METABOLISM occur with aging that affect all body systems, researchers now believe cardiovascular health does not inherently decline simply as a function of aging. DIABETES, OBESITY, lack of physical exercise, and cigarette smoking are the leading causes of acquired CARDIOVASCULAR DISEASE (CVD) among adults. The effects of these factors are cumulative; they are more likely to result in disease the longer they exist and the more of them are present. Accordingly, the risk for acquired cardiovascular disease increases with age because as people get older they tend to develop health conditions that set the stage for cardiovascular deterioration. Most researchers believe these risks are mutable (changeable) through lifestyle.

Cardiovascular Changes at Birth

The cardiovascular system is among the first body systems to develop in the EMBRYO, with the rudimentary HEART beginning to beat at three weeks gestational age. The heart fully forms, and a rudimentary circulatory network develops and functions, by eight weeks gestational age. Before birth, the FETUS draws its oxygen supply from its mother's BLOOD supply, in an exchange that takes place across a membrane in the PLACENTA (fetal

and maternal blood supplies do not mix). Accordingly, the fetal LUNGS do not function. Blood flows to and from the fetus through the umbilical arteries and veins (UMBILICAL CORD).

In the adult heart the right ventricle pumps blood through the PULMONARY ARTERIES to the LUNGS for OXYGENATION. The blood returns to the heart via the PULMONARY VEINS. Because the fetal lungs are nonfunctional, the fetal circulatory system bypasses the lungs. An opening (shunt) between the atria, the foramen ovale, allows blood to flow from the right atrium to the left atrium, which pumps it to the left ventricle. A small amount of blood goes from the right atrium to the right ventricle, which pumps it into the pulmonary ARTERY. A shunt between the aorta and the pulmonary artery, the ductus arteriosus, directs the blood into the aorta where it mixes with the blood the left ventricle pumps into the AORTA. With the first breath following birth the lungs inflate and the changes in pressure initiate a series of biochemical actions that cause these shunts to close, establishing blood circulation through the lungs. Within a few days of birth the ductus arteriosus becomes the ligamentum arteriosum, a strip of connective tissue that stabilizes the aorta and the pulmonary artery. The umbilical veins retreat to form the round ligament supporting the LIVER and the umbilical arteries to form ligaments that support the abdominal muscles.

Cardiovascular Changes at Menopause

Estrogen, the HORMONE responsible for female FERTILITY, is essential for lipid metabolism. The high estrogen levels that mark fertility seem to exert a protective action on a woman's cardiovascular system, lowering the likelihood for HYPERLIPIDEMIA and related health conditions such as ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). During the 35 to 40 years of her fertility, a woman's risk for cardiovascular disease is a third to half that of a man of comparable age and health status. At MENOPAUSE estrogen levels drop significantly and a woman's risk for cardiovascular disease takes a significant jump. Some studies suggest that during the first five years following menopause, a woman's risk for HEART ATTACK is greater than that of a man who is of comparable age and health status.

Hormone replacement therapy (HRT) to restore estrogen levels after menopause became a standard medical approach in the 1950s. In the 1990s numerous studies revealed significant increases in the risks for BREAST CANCER and uterine CANCER associated with HRT as well as failed to find supportive evidence that HRT improved cardiovascular health in women after menopause, and health experts withdrew recommendations for its routine use. Current recommendations suggest women, like men, make nutritious eating choices, get daily physical exercise, maintain healthy weight, and not smoke as the key preventive measures to lower their risk for cardiovascular disease in midlife and beyond.

Lifestyle Choices to Maintain Cardiovascular Health

Current research strongly supports the role of lifestyle choices in maintaining cardiovascular health, even to the extent that many researchers believe appropriate choices beginning in early childhood could prevent as much as 90 percent of acquired cardiovascular disease. Healthy adults who are in their 70s and 80s who do not have any form of cardiovascular disease or other chronic health conditions do not have significant changes in cardiovascular function. Weight management, not smoking, nutritious food choices, and daily physical exercise are the cornerstones of lifestyle measures to preserve cardiovascular health. Many researchers believe the healthy cardiovascular system has the capacity to function efficiently well into the eighth decade of life and beyond.

See also CARDIOVASCULAR DISEASE PREVENTION; CONGENITAL HEART DISEASE; ESTROGENS; LIFESTYLE AND CARDIOVASCULAR HEALTH; LIGAMENT; MUSCLE; PREGNANCY; SMOKING CESSATION; WEIGHT LOSS AND WEIGHT MANAGEMENT.

aneurysm A weakened and often distended (stretched) area in the wall of an ARTERY. Though an aneurysm may develop in any artery, the most common location is the descending or abdominal AORTA. An aneurysm is potentially life-threatening. The continual pressure of the BLOOD flowing through the artery pressures the weakened area, which can cause the layers of the artery's wall to further split and separate, called a dissecting

aneurysm, or to rupture. An aneurysm that ruptures in the BRAIN causes hemorrhagic STROKE, with mild to severe consequences depending on its location and size. Fewer than 5 percent of strokes are hemorrhagic.

Aneurysms sometimes accompany congenital malformations of the blood vessels, called ARTERIOVENOUS MALFORMATIONS (AVMS), in which the arteries and veins in a particular location, usually in the brain or brainstem, form an entangled mass. Aneurysms are also common in MARFAN'S SYNDROME, a genetic disorder that affects the musculoskeletal and cardiovascular systems. Most aneurysms, however, result from atherosclerotic deposits that damage and weaken the walls of the arteries. HYPERTENSION (high BLOOD PRESSURE), when present, exacerbates the situation by exerting further pressure against the weakened area of the artery.

A ruptured aneurysm is a life-threatening emergency that requires immediate medical attention. Loss of blood can be rapid and massive.

Often an aneurysm shows no symptoms. The doctor may detect an aneurysm during a ROUTINE MEDICAL EXAMINATION or during testing or treatment for other medical conditions. Cerebral aneurysms may cause seizures, HEADACHE, or symptoms similar to stroke such as weakness on one side of the body and memory lapses or cognitive dysfunction. An abdominal or thoracic aortic aneurysm may cause PAIN (usually severe) in the area of the aneurysm. These symptoms are usually transient (come and go) though are crucial warning signs that the aneurysm is unstable. Sometimes the doctor can palpate an abdominal aneurysm, feeling its pulsations through the abdominal wall. COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) can affirm the diagnosis. Surgery to repair the aneurysm, in which the surgeon either removes the weakened segment and sutures the healthy ends of the artery together or applies a synthetic patch over the area of weakness, is the only curative treatment. When doctors detect and repair aneurysms before they rupture, they seldom cause further health problems and require no special care after HEALING. It is important to treat the condition that may have caused the aneurysm, when possible, to prevent aneurysms from developing in other locations.

See also ATHEROSCLEROSIS; COGNITIVE FUNCTION AND DYSFUNCTION; CONGENITAL ANOMALY; CORONARY ARTERY DISEASE (CAD); GENETIC DISORDERS; LIFESTYLE AND CARDIOVASCULAR HEALTH; SEIZURE DISORDERS.

angina pectoris Chest discomfort originating from the HEART, usually resulting from restricted BLOOD flow due to CORONARY ARTERY DISEASE (CAD) that occludes (blocks) one or more of the CORONARY ARTERIES. Coronary ARTERY spasm, especially that resulting from COCAINE use, may also cause angina. Some people experience a crushing pressure that radiates into the left shoulder, arm, and THROAT. Other people experience discomfort similar to DYSPEPSIA (indigestion or heartburn). Though the nature and quality of discomfort varies among individuals, for most people angina pectoris is a chronic (long-standing) condition with predictable symptoms that appear with exertion and subside with rest.

An angina pectoris attack lasts only a few minutes, with rest bringing pronounced relief. CHEST PAIN that persists longer suggests HEART ATTACK and requires immediate medical attention.

Angina pectoris does not signal HEART ATTACK, though it is a warning that atherosclerotic accumulations in the coronary arteries have narrowed the arterial lumen (channel or opening through which blood flows) by 70 percent or more. When exercise or other stress (such as stepping out into a cold wind) increases the demand on the heart to pump more blood, the stiffened and narrowed coronary arteries, which in health could expand to nearly double the volume of blood flowing through them, cannot respond. The heart MUSCLE (MYOCARDIUM) fails to receive the oxygen it needs as well as to dispose of the metabolic wastes that are accumulating within its cells.

Treatment for angina pectoris generally combines relieving symptoms and mitigating the underlying cause. Medications to treat angina pectoris cause smooth muscle tissue (such as makes up the walls of the arteries) to relax. This allows

the coronary arteries to modestly increase the flow of blood, which usually is sufficient to ease symptoms. Commonly prescribed medications include nitrates such as nitroglycerin and isosorbide, beta antagonist (blocker) medications such as atenolol and propanolol, and calcium channel antagonist (blocker) medications such as diltiazem and verapamil. Cardiologists typically recommend ASPIRIN THERAPY for people who have angina pectoris, to help prevent MYOCARDIAL INFARCTION (blood clot that blocks the flow of blood, causing heart tissue to die).

For some people, the most effective treatment is ANGIOPLASTY to repair, or CORONARY ARTERY BYPASS GRAFT (CABG) to replace, occluded coronary arteries. However, many people who have angina pectoris remain stable with medication therapy. Cardiologists disagree about the value of CABG for people whose only symptom of disease is angina pectoris, because there is growing evidence that the risks of the surgery (including rapid occlusion of the grafts) do not counterbalance the benefits.

Two forms of angina are more serious: unstable angina and variant angina. In unstable angina, also called acute coronary insufficiency or preinfarction angina, symptoms are unpredictable and do not necessarily correlate to increased demands on the heart such as physical activity may place. Many cardiologists consider unstable angina a precursor to heart attack. With unstable angina, symptoms may occur during sleep or at rest, are often intense and extended, and progressively more severe. Sublingual (under the tongue) nitroglycerin may provide relief. As the underlying heart disease progresses, however, symptoms become more difficult to control. Angioplasty or CABG is often the most viable treatment options.

In variant angina, also called Prinzmetal's angina, spasm of a coronary artery causes symptoms that tend to occur without provocation at certain times of the day. Specific changes in the ELECTROCARDIOGRAM (ECG) accompany the symptoms. Medication (nitroglycerin or calcium channel blocker) is the most effective treatment for most people who have variant angina. CABG may relieve symptoms that do not respond to medication, though typically occlusion affects only one coronary artery to cause the symptoms. Generally the risks of OPEN HEART SURGERY, such that CABG requires, outweigh the potential benefits to replace a single coronary artery. TRANSMYOCARDIAL LASER REVASCULARIZATION (TMLR), a surgical procedure less invasive than CABG that cardiologists began using in 1998, shows promise for relieving angina that does not respond to other treatment. In TMLR, the surgeon uses a laser to pierce the left ventricle with narrow channels. As the channels heal they cause new blood vessels to develop in the myocardium, improving the flow of blood to the heart muscle.

See also INTRA-AORTIC BALLOON PUMP (IABP) COUNTERPULSATION; ISCHEMIC HEART DISEASE; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE.

angiogram A diagnostic test to visualize BLOOD vessels. The test is an angiography; the result is an angiogram. The cardiologist or vascular specialist injects dye into the relevant blood vessels to assess the flow of blood through them, observing the flow via FLUOROSCOPY (moving X-rays). Angiography is useful for diagnosing PERIPHERAL VASCULAR DISEASE (PVD), CORONARY ARTERY DISEASE (CAD), VENOUS INSUFFICIENCY, and DEEP VEIN THROMBOSIS (DVT). The cardiologist does angiography of the HEART during CARDIAC CATHETERIZATION. The risks of angiography include bleeding or INFECTION at the injection site and reaction to the dye. With the precision and availability of noninvasive imaging technology such as COMPUTED TOMOGRAPHY (CT) SCAN and MAGNETIC RESONANCE IMAGING (MRI), doctors use noncardiac angiography (angiography of peripheral blood vessels such as in the legs) primarily when the diagnosis or extent of blockage remains uncertain or before surgery to correct blockages.

See also ANGIOPLASTY; CORONARY ARTERY BYPASS GRAFT (CABG).

angioplasty A CARDIAC CATHETERIZATION procedure to widen the opening of an ARTERY, generally as treatment for ANGINA PECTORIS, CORONARY ARTERY DISEASE (CAD), or PERIPHERAL VASCULAR DISEASE (PVD). Angioplasty is most effective when the occlusion is between 70 percent and 90 percent and affects only one or two locations within the arteries. More extensive occlusion in the coronary arteries may require CORONARY ARTERY BYPASS GRAFT (CABG) to instead redirect the blood flow through replace-

ment arteries. The cardiovascular surgeon may also use angioplasty to remedy occlusions in arteries other than those supplying the HEART, such as to treat PVD affecting the larger arteries in the legs.

Procedure

Angioplasty is almost always an AMBULATORY SURGERY (same-day) procedure, or at most requires one night in the hospital for recovery and observation following the procedure. The cardiologist uses local ANESTHETIA and general SEDATION to make the person comfortable. After numbing the location with local anesthetic the cardiologist inserts a catheter into an ARTERY near the surface of the body, typically the femoral artery in the groin, and threads it into the occluded artery. Injected dye helps the cardiologist to visualize the catheter's progress using FLUOROSCOPY (moving X-ray), which displays the images on a closed circuit monitor.

Once the catheter is in position at the occlusion, the cardiologist uses a syringe to inject a small amount of sterile solution through the catheter to inflate a tiny balloon at the catheter's tip. The balloon applies pressure against the walls of the artery, expanding the channel through which blood flows. The cardiologist may deflate the balloon, advance the catheter, and reinflate the balloon to widen a larger segment of the artery. The procedure usually compresses accumulations of ATHEROSCLEROTIC PLAQUE (atheromas) to reduce their intrusion into the arterial passageway. The cardiologist may also use the catheter to place a STENT, a tiny springlike device that maintains pressure against the arterial wall to help maintain the widened channel in the artery at the site of the compressed atheroma.

Risks and Complications

Risks during the angioplasty include HEART ATTACK or STROKE from dislodged atherosclerotic plaque (which is rare), excessive bleeding, trauma to the artery, and irritation of the heart that causes ARRHYTHMIA. The cardiac catheterization facility or hospital where the cardiologist performs the angioplasty is equipped and staffed for immediate cardiac surgery if necessary. More common complications are bleeding and PAIN at the catheter insertion site, or INFECTION following the procedure. The cardiologist may choose to administer prophylactic ANTIBIOTIC MEDICATIONS, particularly in people who are at risk for bacterial ENDOCARDITIS.

The most common complication of angioplasty is restenosis (reclosure) of the artery, either from the compressed atheroma reexpanding or from continued atherosclerotic processes that create new atheromas. About half of people who undergo angioplasty experience restenosis within two years. About a quarter have clinically significant restenosis within six months and must have a repeat angioplasty or CABG to restore blood flow to the heart. Repeat angioplasty is generally less successful, and carries a higher risk of damage to the artery. As atherosclerosis progresses, which it tends to do, other coronary arteries occlude as well.

Outlook and Lifestyle Modifications

Angioplasty is a temporary measure for most people, providing relief of symptoms for six months to two or three years. However, angioplasty does not treat the underlying disease process, which is likely to continue even with medical interventions such as lipid-lowering medications to slow its progress. Most arteries tend to reocclude. Some people are able to undergo multiple angioplasty procedures over time though others must look to different treatment options such as CABG. The most effective outcomes are those that follow the angioplasty with lifestyle changes to improve cardiovascular health such as WEIGHT LOSS AND WEIGHT MANAGEMENT, daily physical activity, and SMOKING CESSATION.

See also ATHERECTOMY; DIABETES AND CARDIOVASCULAR DISEASE; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT.

anticoagulation therapy Prophylactic (preventive) treatment with medications to reduce the risk of BLOOD clots, broadly including approaches that inhibit various stages of COAGULATION. Anticoagulation therapy is common treatment for a number of cardiovascular conditions including ATRIAL FIBRILLATION, INTERMITTENT CLAUDICATION, DEEP VEIN THROMBOSIS (DVT), PULMONARY EMBOLISM, and VALVULAR HEART DISEASE, and following MYOCARDIAL INFARCTION (HEART ATTACK) and cerebral infarction (ischemic or thromboembolic STROKE). Anticoagulant medications prevent new clots from forming

and existing clots from getting larger, though cannot dissolve clots that already exist. Medications that dissolve existing clots are called thrombolytic agents, which have different pharmacologic actions in the body.

The appropriate anticoagulation therapy depends on the reason for the therapy (health condition), the person's overall health situation, and any other medications the person needs to take. Doctors may prescribe anticoagulation therapy for noncardiovascular reasons such as after orthopedic surgery, particularly JOINT REPLACEMENT. People commonly refer to anticoagulant medications as "blood thinners," though this is a misnomer because these medications do not alter the blood's viscosity (thickness).

Antiplatelet Agents

Antiplatelet medications, also called PLATELET inhibitors, slow clot formation by inhibiting PLATELET AGGREGATION. These medications are especially effective in people who have increased risk for CORONARY ARTERY DISEASE (CAD) or thromboembolic stroke. Platelets are the cells in the blood that are first on the scene of any injury in the body. They swarm in response to even the slightest of damage, such as the irritation and INFLAMMATION atheromas cause to the walls of the arteries. When they aggregate, or clump together, they release chemical signals that activate the sequence of events resulting in clot formation. Antiplatelet medications interfere with these chemical signals.

The most commonly used antiplatelet therapy is ASPIRIN THERAPY. Aspirin inhibits PROSTAGLANDINS, chemicals that platelets require to enable them to aggregate or stick together. Aspirin delays clotting by delaying platelet aggregation, which is the first step in the coagulation process. Platelets may come together but not stick, drifting away from each other again before they initiate the clotting process. Other commonly prescribed antiplatelet medications include clopidogrel (Plavix), ticlopidine (Ticlid), dipyridamole (Persantine), and cilostazol (Pletal). These medications may have serious side effects or interact with other medications. Ticlopidine may cause a rare but life-threatening condition, thrombotic thrombocytopenic purpura (TTP), and requires frequent blood tests to monitor for its development.

Clotting Factor Inhibitors

Other medications act to interfere with the body's ability to activate blood proteins essential for clotting (CLOTTING FACTORS). The most commonly used oral medication, warfarin (Coumadin), works by blocking one of the steps in the body's process to produce VITAMIN K. Vitamin K is essential to the metabolic processes that activate clotting factors II, VII, IX, and X. The gastrointestinal tract does not absorb heparin, which is available only in injectable form (intravenous or subcutaneous). Heparin prevents the conversion of prothrombin (clotting factor II) to thrombin, a crucial and early step of coagulation. Both of these medications are NARROW THERAPEUTIC INDEX (NTI) drugs that require very close monitoring to maintain their doses within therapeutic range. Internal bleeding, especially from the gastrointestinal tract, can occur when doses are too high. Excessive bleeding from wounds, such as ACCIDENTAL INJURIES, or from routine dental procedures, such as prophylactic cleaning, is also a risk.

Low molecular weight heparin (LMWH), also only in injectable form, acts similarly to heparin though without many of heparin's undesired side effects. Several kinds of LMWH, also called fractionated heparin, are available. Each has unique characteristics and though all are LMWH drugs, they are not interchangeable. LMWH products include dalteparin (Fragmin), enoxaparin (Lovenox), and tinzaparin (Innohep). Another injectable medication, fondaparinux (Arixtra), inhibits clotting factor X. Proper site selection and injection technique are important for people who use injectable forms of anticoagulant medications.

Benefits, Risks, and Lifestyle Modifications

Anticoagulant medications, whether antiplatelet or inhibitor, are preventive for blood clots and the health problems blood clots can cause, such as stroke, HEART attack, pulmonary embolism, and DVT. The primary risk of anticoagulation therapy is excessive or prolonged bleeding, which can be serious or life-threatening in some situations. Doctors carefully monitor blood clotting times and other measures to maintain an appropriate therapeutic balance. Spontaneous nosebleed (EPISTAXIS), easy bruising, bleeding from the gums when brushing the teeth, and blood in the stool are signs

ANTICOAGULANT MEDICATIONS

Medication	Action	Common Reasons Prescribed
aspirin	antiplatelet	HEART ATTACK and STROKE PROPHYLAXIS ATRIAL FIBRILLATION
cilostazol	antiplatelet	INTERMITTENT CLAUDICATION PERIPHERAL VASCULAR DISEASE (PVD)
clopidogrel	antiplatelet	heart attack and stroke prophylaxis atrial fibrillation
dalteparin	clotting factor inhibitor; low molecular weight heparin (LMWH)	DEEP VEIN THROMBOSIS (DVT) and PULMONARY EMBOLISM (PE) prophylaxis after major surgery that limits mobility during recovery
dipyridamole	antiplatelet	in combination with aspirin for heart attack and stroke prophylaxis in combination with warfarin after heart valve replacement to prevent clots from forming on the prosthetic valve
enoxaparin	clotting factor inhibitor; LMWH	DVT and PE prophylaxis after major surgery that limits mobility during recovery
fondaparinux	clotting factor inhibitor; blocks clotting factor X	DVT and PE prophylaxis after major surgery that limits mobility during recovery
heparin	clotting factor inhibitor	during OPEN HEART SURGERY after major surgery that limits mobility during recovery DVT and PE prophylaxis
ticlopidine	antiplatelet	stroke prophylaxis in people who cannot take aspirin or who have had previous strokes
tinzaparin	clotting factor inhibitor; LMWH	DVT and PE prophylaxis after major surgery that limits mobility during recovery
warfarin	clotting factor inhibitor; blocks VITAMIN K SYNTHESIS	intermittent claudication PVD atrial fibrillation

of excessive anticoagulation that require a doctor's evaluation.

When on anticoagulation therapy it is important to avoid OVER-THE-COUNTER (OTC) DRUGS such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) in products for PAIN relief, menstrual cramps, and cold and flu relief, and salicylates such as Pepto-Bismol. These products have mild anticoagulation effects that can cause excessive bleeding in combination with anticoagulation medications. As well, anticoagulation medications interact with numerous other medications and may have side effects, some of which can have serious health consequences.

Many people who are on anticoagulation therapy have underlying cardiovascular conditions that would benefit from lifestyle modifications as well, such as increased physical activity and SMOKING CESSATION. Regularly stretching the muscles throughout the day, especially leg muscles, and walking for 5 to 10 minutes every few hours help keep blood from pooling and clotting.

See also ARRHYTHMIA; GASTROINTESTINAL BLEEDING; LIFESTYLE AND CARDIOVASCULAR HEALTH; THROMBOCYTOPENIA; THROMBOLYTIC THERAPY.

aorta The ARTERY that carries BLOOD from the HEART to the body. The largest blood vessel in the body, the aorta arises from the left ventricle. At its widest point the aorta is about one and a half inches in diameter. As the aorta leaves the heart it ascends to curve behind the right atrium. The first arteries to branch from the base of the ascending aorta are the right and left CORONARY ARTERIES that supply the heart MUSCLE (MYOCARDIUM) with blood. Branching from the arch as the aorta crests over the heart are the three arteries that carry blood to the upper body:

- the brachiocephalic artery (also called the innominate artery), which transports blood to the right arm and right side of the BRAIN, head, and face
- the left common carotid artery, which transports blood to the left side of the brain, head, and face
- the left subclavian artery, which transports blood to the left arm

The aorta then crosses over the PULMONARY ARTERIES and drops behind the heart to descend through the chest and into the abdomen, aligned along the front of the spine, branching into the iliac arteries at the top of the pelvis. Numerous arteries branch from the descending aorta along its passage from the chest to the abdomen, supplying vital organs such as the LIVER, kidneys, STOMACH, and intestines. Acquired cardiovascular conditions that can affect the aorta include ATHEROSCLEROSIS, ANEURYSM, and AORTIC STENOSIS. A number of congenital malformations also can affect the aorta, including aortic coarctation, tetralogy of Fallot, and transposition of the great arteries (TPA). Most aortic conditions require surgical repair.

For further discussion of the aorta within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also CONGENITAL HEART DISEASE; PULMONARY VEINS; VENA CAVA.

aortic stenosis Narrowing of the aortic valve that restricts the flow of BLOOD from the heart's left ventricle to the AORTA. Aortic stenosis may be congenital or acquired; in either, it tends to show symptoms later in life. Acquired aortic stenosis develops as a consequence of calcium and arterial plaque deposits that infiltrate the aortic valve. Untreated aortic stenosis results in left ventricular hypertrophy (enlargement of the left ventricle), diminished CARDIAC OUTPUT, and ultimately congestive HEART FAILURE.

Symptoms of aortic stenosis may include PALPITATIONS, ANGINA PECTORIS, fatigue, SYNCOPE (fainting), and unexplained inability to participate in aerobic activities. The diagnostic path typically includes ECHOCARDIOGRAM and CARDIAC CATHETERIZATION. Treatment is surgery to replace the damaged aortic valve. After valve replacement most people experience dramatic relief from symptoms and are able to return to regular activities. Sometimes medications are necessary to treat companion conditions such as HEART failure. As with other valve operations, aortic valvuloplasty or prosthesis increases the risk for blood clots to form. Most people will need to take ANTICOAGULATION THERAPY to mitigate this risk.

See also ANTIBIOTIC PROPHYLAXIS; CONGENITAL HEART DISEASE; RHEUMATIC HEART DISEASE; VALVULAR HEART DISEASE.

apolipoprotein B100 (apoB100) A protein on the surface of lipid molecules that directs the lipid's route of METABOLISM. ApoB100 occurs primarily on low-density lipoprotein (LDL) molecules, the form of cholesterol with the highest risk for CORONARY ARTERY DISEASE (CAD). The normal level of apoB100 in the blood is 40 to 125 milligrams per deciliter (mg/dL). Elevated levels suggest familial HYPERLIPIDEMIA. ApoB100 levels also rise after MYOCARDIAL INFARCTION, when there is

damage to the HEART MUSCLE. Elevated apoB100 levels convey an increased risk for ATHEROSCLEROSIS and CAD.

See also CARDIOVASCULAR DISEASE PREVENTION; CHOLESTEROL BLOOD LEVELS; HYPERLIPIDEMIA; RISK FACTORS FOR CARDIOVASCULAR DISEASE.

arrhythmia Irregularity or abnormality of the heart's contractions. Arrhythmias can result from numerous causes including electrical disturbances of the heart's pacing mechanisms, physical damage to the HEART such as might occur with HEART ATTACK, interruptions of the heart's BLOOD supply that cause myocardial HYPOXIA (oxygen depletion), severe electrolyte imbalances, and medication side effects. COCAINE use can initiate sudden and fatal arrhythmias. Because all myocardial cells have the ability to initiate electrical impulses, it is sometimes difficult for cardiologists to determine what causes an arrhythmia.

The most common kinds of arrhythmias are

- bradycardia, in which contractions are slower than normal (typically fewer than 60 beats per minute at rest in a person whose level of routine physical activity is low)
- tachycardia, in which contractions are faster than normal (typically greater than 100 beats per minute at rest in a person whose level of routine physical activity is low)
- fibrillation, in which contractions are rapid, erratic, and nonproductive
- premature or extra beats, in which contractions occur in addition to the heart's regular contractions

The seriousness of an arrhythmia depends largely on whether it is atrial or ventricular. Typically ventricular arrhythmias are more significant and potentially hazardous than atrial arrhythmias. The most common arrhythmia that requires treatment is ATRIAL FIBRILLATION, which health experts estimate affects about one in five American adults over age 60 and which accounts for about 15 percent of strokes. The most deadly arrhythmia is VENTRICULAR FIBRILLATION, which results in seriously slowing or even halting the flow of blood to the body because the ventricles cannot pump in a coordinated manner. Some arrhythmias are transient (come and go), and others cause no symptoms or effect on cardiovascular function.

VENTRICULAR FIBRILLATION is a medical emergency that can result in death within minutes without appropriate treatment (DEFIBRILLATION).

Symptoms and Diagnostic Path

Arrhythmias may cause a range of symptoms or no symptoms at all. The most common symptoms are

- PALPITATIONS, which feel like the heart is thumping or "skipping" a beat
- weakness, lightheadedness, or fainting
- shortness of breath with exertion (DYSPNEA)
- CHEST PAIN

It is not possible to know only from the symptoms what kind of arrhythmia is present. Only an ELECTROCARDIOGRAM (ECG), a test that records the heart's electrical activity, can present the information a cardiologist needs to determine the diagnosis. The cardiologist may desire further diagnostic procedures to identify any underlying causes, as the findings may influence treatment options and decisions. Arrhythmias resulting from CORONARY ARTERY DISEASE (CAD) or HEART FAILURE, for example, require different treatment than those resulting from idiopathic electrical disturbances (problems with the heart's pacing mechanisms that have no apparent cause). Occasionally the doctor detects an arrhythmia during examination for other health concerns, which requires subsequent evaluation to determine whether, as it is not causing symptoms, it is a condition that warrants treatment.

Treatment Options and Outlook

CAFFEINE and ALCOHOL consumption can cause palpitations and other minor, benign arrhythmias, as can intense stress. Making lifestyle changes to reduce or eliminate these factors typically ends the arrhythmias related to them. Arrhythmias that are not clinically significant (those that cause no symptoms or disruptions of cardiovascular function) do not require treatment, though cardiologists generally want to monitor them to make sure

they remain benign. Antiarrhythmia medications successfully treat the majority of symptomatic arrhythmias. These medications work by blocking certain aspects of the biochemical functions responsible for myocardial contractions. The cardiologist may prescribe two or more antiarrhythmia medications in combination to treat some kinds of arrhythmias. People who have heart failure, CAD, valvular disease, and other heart disorders may take antiarrhythmia medications along with other medications to treat these conditions.

Cardiologists select antiarrhythmia medications based on the characteristics of the arrhythmia, which may be simple or complex, as well as the presence of other cardiovascular conditions, any other medications the person may be taking, and factors such as age and lifestyle. After starting antiarrhythmia therapy, it is important to continue until the cardiologist makes changes in the therapeutic approach. Suddenly stopping an antiarrhythmia medication can have significant consequences including serious arrhythmias.

Antiarrhythmia medications can have serious side effects such as worsening the existing arrhythmia or causing new arrhythmias. Some medications work by causing heart block, for example, to interrupt the conduction of aberrant electrical impulses. Finding the right medication or combination of medications sometimes takes a period of trial regimens and dosages. As the condition responsible for the arrhythmia changes over time, sometimes it becomes necessary to change the medication regimen as well.

Other interventions may become necessary if medications are ineffective or generate intolerable side effects. Such interventions may include

- CARDIOVERSION, in which the cardiologist delivers (under sedation) a mild electrical shock through the chest wall to reorganize and restore to normal the heart's electrical activity
- RADIOFREQUENCY ABLATION, a cardiac catheterization procedure in which the cardiologist uses radiofrequency impulses to kill a small and carefully targeted segment of myocardial cells to prevent them from initiating or conveying electrical impulses
- implantable PACEMAKER, a small battery-operated device that emits an electrical impulse to trigger the heart's contractions

COMMONLY PRESCRIBED ANTIARRHYTHMIA MEDICATIONS

Beta Blockers		
acebutolol (Sectral)	atenolol (Tenormin)	betaxolol (Kerlone)
carteolol (Cartrol)	esmolol (Brevibloc)	labetalol (Normodyne)
metoprolol (Lopressor)	nadolol (Corgard)	penbutolol (Levatol)
pindolol (Visken)	propranolol (Inderal)	sotalol (Betapace)
timolol (Blocadren)		
Calcium Channel Blockers		
amlodipine (Norvasc)	bepridil (Vascor)	diltiazem (Cardizem)
felodipine (Plendil)	isradipine (DynaCirc)	nicardipine (Cardene)
nifedipine (Procardia)	nimodipine (Nimotop)	nisoldipine (Sular)
verapamil (Isoptin)		
Miscellaneous Actions		
adenosine	digoxin	
Potassium Channel Blockers		
amiodarone (Cordarone)	dofetilide (Tikosyn)	ibutilide (Corvert)
Sodium Channel Blockers		
disopyramide (Norpace)	flecainide (Tambocor)	lidocaine (Xylocaine)
mexiletine (Mexitil)	moricizine (Ethmozine)	procainamide (Procan)
propafenone (Rythmol)	quinidine (Cardioquin)	tocainide (Tonocard)

- IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD), which functions both to deliver pacing impulses and shocking impulses to convert an arrhythmia that extends beyond certain parameters

Most people are able to successfully control or eliminate arrhythmias with appropriate treatment, resulting in no changes to lifestyle or quality of life.

Risk Factors and Preventive Measures

Most arrhythmias arise as a consequence of other CARDIOVASCULAR DISEASE (CVD) or are idiopathic (without identifiable cause). Some arrhythmia disorders are congenital or genetic, such as LONG QT SYNDROME (LQTS). People who have one kind of arrhythmia are prone to developing others. Prompt medical evaluation of symptoms that could signal cardiovascular disease or arrhythmias is important, as early detection and treatment may head off consequences such as CARDIAC ARREST or SUDDEN CARDIAC DEATH.

See also AUTOMATED EXTERNAL DEFIBRILLATOR (AED); BUNDLE BRANCH BLOCK; CARDIOPULMONARY RESUSCITATION (CPR); GENERIC DRUG; PAROXYSMAL ATRIAL TACHYCARDIA (PAT); PREMATURE VENTRICULAR CONTRACTION; STRESS AND STRESS MANAGEMENT; STROKE; TORSADE DE POINTES; WOLFF-PARKINSON-WHITE SYNDROME.

arteriosclerosis A degenerative condition of the arteries in which the walls of the arteries become stiff and rigid. Arteriosclerosis is a leading factor in age-related HYPERTENSION (high BLOOD PRESSURE). There are three forms of arteriosclerosis:

- ATHEROSCLEROSIS in which arterial plaque deposits infiltrate the inner layer of the arterial wall
- Mönckeberg's arteriosclerosis or medial calcific sclerosis, in which the medial layer of the arterial wall accumulates calcium deposits that cause the ARTERY to become rigid
- arteriolosclerosis in which the arterioles (the threadlike arteries that form the arterial portion of the CAPILLARY BEDS) lose their FLEXIBILITY and elasticity

The primary causes of arteriosclerosis include cigarette smoking (NICOTINE is highly toxic to the smooth MUSCLE fibers of the arteries), DIABETES, and hypertension. The consequences of arteriosclerosis, particularly atherosclerotic, include increased risk for HEART ATTACK, STROKE, ANEURYSM, and increased hypertension. People often use the terms atherosclerosis and arteriosclerosis interchangeably, which is not quite accurate though is correct about 90 percent of the time because atherosclerosis is the most common form of arteriosclerosis.

See also DIABETES AND CARDIOVASCULAR DISEASE; HYPERLIPIDEMIA; LIFESTYLE AND CARDIOVASCULAR HEALTH.

arteriovenous malformation (AVM) A congenital deformity in which an entanglement of arteries and veins forms. Rather than connecting into CAPILLARY BEDS that form between them, the arteries and veins in an AVM connect directly to one another. Veins lack the structure to accommodate the pressure BLOOD is under as it flows through the arteries and over time may become weakened and rupture. The resulting bleeding can be life-threatening, depending on the size and location of the AVM. Most AVMs are in the BRAIN, although an AVM can occur in other parts of the body. Though AVMs are present at birth, many do not show symptoms until later in life, even adulthood.

The symptoms of AVM vary and often are vague, making diagnosis sometimes difficult. Cerebral AVMs (AVMs in the brain) may cause HEADACHE, seizures, and STROKE-like symptoms if they apply pressure to surrounding brain tissue or if they bleed. HEMORRHAGE in the brain can cause permanent damage to the brain, resulting in PARALYSIS, cognitive loss, or death. AVMs elsewhere in the body may cause PAIN or bleeding; hemorrhagic bleeding is life-threatening. COMPUTED TOMOGRAPHY (CT) SCAN and magnetic resonance angiography, which combines MAGNETIC RESONANCE IMAGING (MRI) with dye injected into the blood vessels, are the key diagnostic procedures to detect AVM.

Treatment depends on the size and location of the AVM and may include surgery to remove the web of blood vessels, injection of a substance to block the flow of blood through the AVM (embolization), or RADIOFREQUENCY ABLATION to close off the blood vessels. Treatment often carries signif-

icant risk of uncontrolled bleeding because of the unstable nature of the AVM, and sometimes the risk of attempting treatment is greater than the risk of leaving the AVM untreated. Treatment that successfully removes or seals the AVM ends the threat of hemorrhage.

See also ANEURYSM; ARTERY; BIRTH DEFECTS; CONGENITAL ANOMALY; VEIN.

artery A flexible, muscular BLOOD vessel that carries blood from the HEART and oxygenated blood to tissues throughout the body. The wall of an artery has three layers:

- adventitia, the outermost layer, which is primarily connective tissue that gives the artery its FLEXIBILITY
- media, the middle layer, which is mostly smooth MUSCLE tissue that gives the artery the ability to contract and relax
- intima, the inner layer, which is epithelial tissue that provides a smooth surface to facilitate the flow of blood

The adventitia is more prominent in larger arteries such as the AORTA and the carotid arteries, encasing the artery in a weblike fashion without clear direction to its fibers. In smaller arteries, the media often dominates the artery's structure. The muscle fibers of the media encircle the artery, helping strengthen and stabilize the artery's walls. The delicate intima contains two structural levels, the basement or foundation membrane and the subepithelial layer, both of which run lengthwise. Each may be only a cell's thickness in small arteries, indistinguishable without magnification.

The intima's two-level structure gives the artery its ability to carry blood cells without having them stick to its inner walls. However, it also makes the artery vulnerable to ATHEROSCLEROSIS, which develops between the intima's two levels. The tiniest of the body's arteries, about the thickness of a hair, are arterioles. The body's largest artery is the aorta, which carries blood from the heart to the network of arteries that then carry the blood throughout the body.

Fibrous sheaths enclose most of the body's arteries, usually along with the companion VEIN and NERVE. These sheaths often parallel skeletal structures for protection and stability, or run deep within the body. Arteries also receive blood themselves from other arteries, which deliver oxygen and other nutrients to the layers of the artery, and contain nerves that deliver the signals to constrict or dilate. The walls of the arteries constrict and dilate in wavelike contractions that coordinate with the heartbeat to help push blood through the body. These pulsations are detectable as the PULSE at points where the artery is near the surface of the skin, such as at the wrist and the groin.

For further discussion of the artery within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also ARTERIOVENOUS MALFORMATION (AVM); ATHEROSCLEROSIS; ARTERIOSLCEROSIS; CAROTID BRUIT; CAROTID STENOSIS; CORONARY ARTERY DISEASE (CAD).

aspirin therapy A form of ANTICOAGULATION THERAPY to help prevent BLOOD clots from developing, which doctors prescribe as a prophylactic measure for HEART ATTACK and STROKE. Aspirin has a moderate anticoagulation effect. It interferes with PLATELET AGGREGATION, the first step in the clotting process. Aspirin blocks the body's production of PROSTAGLANDINS, chemicals the platelets need to help them aggregate (clump together). Cardiologists generally recommend aspirin therapy for:

- men between the ages of 40 and 75
- women who are beyond MENOPAUSE
- men and women under age 40 who have HYPERTENSION, DIABETES, or OBESITY
- men and women under age 40 who smoke cigarettes

People who do not have increased risk for CARDIOVASCULAR DISEASE (CVD)—are under age 40 and have no predisposing health conditions or lifestyle factors—likely do not receive enough benefit from aspirin therapy to offset the potential risks. The primary risks of aspirin therapy are gastrointestinal upset and excessive bleeding. Aspirin may cause GASTROINTESTINAL BLEEDING in people who have PEPTIC ULCER DISEASE, and extended bleeding during dental procedures and surgeries or with wounds such as lacerations. Doctors recommend a DOSE of

81 milligrams (mg) daily (one "baby" aspirin tablet) or 325mg milligrams every other day (one "regular" aspirin). Some products are available at 162mg strength, marketed specifically for aspirin therapy.

Call 911 at the first sign of HEART ATTACK. Do not wait for an aspirin to relieve the PAIN of a heart attack. An aspirin will only help to limit blood clotting during the heart attack. It will not help the pain.

Aspirin may also limit the damage of a HEART attack that is under way. Cardiologists recommend that people who experience symptoms of heart attack first call 911 for emergency medical aid and then chew an aspirin tablet. Chewing the aspirin tablet gets it into the bloodstream more quickly than swallowing. Studies show this approach releases enough of a burst of anticoagulant into the blood to help prevent fibrin and other clotting substances from adhering to the blockage in the coronary artery that is causing the symptoms. This small action can significantly reduce the amount of heart tissue that suffers oxygen deprivation and possible death during a heart attack.

See also CARDIOVASCULAR DISEASE PREVENTION; CORONARY ARTERIES; DEEP VEIN THROMBOSIS (DVT); RISK FACTORS FOR CARDIOVASCULAR DISEASE.

atherectomy A surgical procedure, done via CARDIAC CATHETERIZATION, to remove patches of arterial plaque (ATHEROSCLEROTIC PLAQUE), called atheromas, from the inner walls of major arteries such as the CORONARY ARTERIES. The cardiologist uses either a laser to vaporize or a rotary burr on the end of the catheter to shave away the atheromas. Often the cardiologist follows the atherectomy with balloon ANGIOPLASTY and STENT placement to help keep the ARTERY open, as atheromas tend to redevelop. Risks of atherectomy include STROKE and HEART ATTACK from debris particles that break away and become lodged in the arteries of the BRAIN or the HEART.

See also ENDARTERECTOMY; SURGERY BENEFIT AND RISK ASSESSMENT.

atherosclerosis Accumulation of lipids and other materials (ATHEROSCLEROTIC PLAQUE) between the two layers of an artery's inner wall, the intima. Over time the accumulations form brittle, hard deposits called atheromas that thicken the intima and the media (the middle of the arterial wall's three layers). The usual consequence is that the ARTERY becomes stiff and less flexible, and its inner channel, the lumen, narrows. The combined effect limits the ability of the artery to dilate or constrict, increasing the pressure necessary to push BLOOD through the artery. The result is CARDIOVASCULAR DISEASE (CVD), including HYPERTENSION (high BLOOD PRESSURE), CORONARY ARTERY DISEASE (CAD), and PERIPHERAL VASCULAR DISEASE (PVD). Atherosclerosis takes decades to develop. Many researchers believe the process of atherosclerotic accumulation begins in late childhood.

Atherosclerosis will most commonly affect medium-size arteries such as the CORONARY ARTERIES that supply the HEART, the carotid arteries that supply the BRAIN, and the primary arteries that supply the legs. Atherosclerosis can also develop in the large arteries, notably the AORTA. Atherosclerosis in the aorta presents a significant risk for aortic ANEURYSM, a potentially life-threatening circumstance in which the walls of the aorta weaken and begin to separate. The most significant risk of atherosclerosis, however, is HEART ATTACK or STROKE, resulting from particles of atherosclerotic plaque that break free and become lodged in an artery. The blockage may occur at the location of the occlusion or at a distant site. Blood clots also may form at the sites of the plaque accumulations (atheromas), occluding the artery at the site or, like the plaque particles, breaking free and becoming lodged elsewhere in the body.

Symptoms and Diagnostic Path

Atherosclerosis typically does not present symptoms until it advances to a further disease state such as CAD or hypertension resulting from renal artery stenosis. A key indicator that atherosclerosis exists, however, is elevated blood lipid (cholesterol and triglycerides) levels. Cardiologists generally perceive a total blood cholesterol level of 200 as indicating that there is some degree of atherosclerotic disease present. Lowering CHOLESTEROL BLOOD LEVELS reduces the risk for further atherosclerotic deposits and can also reverse to some extent atherosclerotic disease that already exists. The diag-

nostic path typically includes CARDIAC CATHERIZATION or vascular catheterization, which allows the cardiologist to directly visualize the extent of atherosclerotic disease present. ELECTRON BEAM COMPUTED TOMOGRAPHY (EBCT) SCAN, a noninvasive imaging procedure, shows promise for identifying atherosclerosis in its early stages. EBCT detects calcium in the atherosclerotic deposits.

Treatment Options and Outlook

Treatment may target the damaged arteries, the underlying disease process, or both. Treating the damaged artery generally takes precedence as the atherosclerotic occlusions restrict and may even block the flow of blood.

Risk Factors and Preventive Measures

The primary risk factor for atherosclerosis is elevated cholesterol blood levels, which allow fatty acids to accumulate in the blood. Cigarette smoking, OBESITY, hypertension, and DIABETES further increase the risk for atherosclerosis. Cigarette smoking and hypertension alter the cells of the arterial walls in ways that reduce their FLEXIBILITY, making them more susceptible to atherosclerotic accumulations. Diabetes and obesity both alter lipid METABOLISM. Preventive measures include a diet with fewer than 10 percent of its CALORIES from saturated fats (such as meats), daily physical exercise, SMOKING CESSATION, and WEIGHT LOSS AND WEIGHT MANAGEMENT. Health experts encourage people to develop heart-healthy lifestyle habits early in life, as so much research now confirms that the cardiovascular diseases common in people who are in their 60s and beyond get their start in the teenage years or earlier.

See also CALORIE; CARDIOVASCULAR DISEASE PREVENTION; DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND CARDIOVASCULAR HEALTH; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; PULMONARY EMBOLISM.

atherosclerotic plaque Debris that collects within the inner layer of the wall of an artery, also called arterial plaque. Atherosclerotic plaque typically includes fatty acids, dead cells, platelets, and other particles such as proteins and minerals (notably calcium, which gives the plaque its stiffness). The fatty acids, such as cholesterol and triglycerides, are heavy and sticky. The flow of the BLOOD pushes them to the outer edges, up against the arterial walls. Initially the debris is a minor irritation to the inner surface of the arteries. Over time, however, the irritation creates INFLAMMATION that attracts further debris. The sticky nature of the debris in combination with the inflammation establishes a circumstance in which the debris becomes embedded within the intima, the inner layer of the arterial wall, creating deposits called atheromas and evolving into the disease state of ATHEROSCLEROSIS. Atherosclerotic plaque in the CORONARY ARTERIES becomes CORONARY ARTERY DISEASE (CAD) and in other arteries becomes PERIPHERAL VASCULAR DISEASE (PVD).

See also CAROTID STENOSIS; CHOLESTEROL BLOOD LEVELS; HYPERLIPIDEMIA; LIFESTYLE AND CARDIOVASCULAR HEALTH; PLATELET; TRIGLYCERIDE BLOOD LEVEL.

atrial fibrillation An ARRHYTHMIA in which the upper chambers of the HEART, the atria, contract rapidly and out of synchronization with each other. As a consequence, they do not pump BLOOD very effectively to the ventricles. Though most of the blood that enters the atria drains to the ventricles, some blood pools in the atria. The pooled blood establishes a very high risk for blood clots to form and a corresponding increase in the risk of STROKE or TRANSIENT ISCHEMIC ATTACK (TIA). Atrial fibrillation is the cause of one in five strokes. Atrial fibrillation is the most common arrhythmia that requires treatment, affecting about 5 percent of people over age 65.

The typical symptoms of atrial fibrillation include

- PALPITATIONS
- rapid tiring during physical activity
- generalized fatigue
- DYSPNEA (shortness of breath)
- ANGINA PECTORIS (CHEST PAIN)
- SYNCOPE (fainting)

However, many people have mild or no symptoms, with the doctor detecting atrial fibrillation during the course of examination for other health concerns.

HYPOTENSION (low BLOOD PRESSURE) and a weak, irregular, and often rapid PULSE are common signs

the doctor detects during examination. An ELECTROCARDIOGRAM (ECG) confirms the diagnosis. ECHOCARDIOGRAM may reveal the underlying cause of the arrhythmia, especially when VALVULAR HEART DISEASE is to blame. Antiarrhythmia medications such as beta blockers or calcium channel blockers restore a normal heart rhythm (normal sinus rhythm) in most people who have atrial fibrillation. These medications can have mild to significant side effects and can slow the heart too much, causing bradycardia, another arrhythmia.

For atrial fibrillation that does not respond to these medical measures, the cardiologist may suggest CARDIOVERSION, which uses electrical shock to jolt the heart back into normal rhythm, or RADIOFREQUENCY ABLATION, which destroys a small portion of heart tissue to permanently disrupt the flow of electrical impulses in the heart. Cardiologists typically prescribe ANTICOAGULATION THERAPY, usually aspirin or warfarin and sometimes both, in addition to antiarrhythmia medications for people who have atrial fibrillation, to reduce the risk for clot formation and resulting stroke.

Common causes of atrial fibrillation include HYPERTENSION (high blood pressure), CORONARY ARTERY DISEASE (CAD), congestive HEART FAILURE, PERICARDITIS, and RHEUMATIC HEART DISEASE. Atrial fibrillation may follow MYOCARDIAL INFARCTION and is also more common among people who have DIABETES or HYPERTHYROIDISM. There are no known measures for preventing atrial fibrillation beyond lifestyle behaviors to maintain overall cardiovascular health.

See also GALLOP; LIFESTYLE AND CARDIOVASCULAR HEALTH; LONG QT SYNDROME (LQTS); MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; WOLFF-PARKINSON-WHITE SYNDROME.

atrioventricular (AV) node A cluster of electrical fibers in the HEART that focuses and intensifies the electrical impulses the SINOATRIAL (SA) NODE initiates. The SA node, a cluster of specialized NERVE fibers at the top of the right atrium near the superior VENA CAVA, is the heart's natural PACEMAKER. It generates a rhythmic electrical impulse that spreads through the myocardial cells of the right atrium. The AV node, located at the base of the right atrium at its juncture with the right ventricle, gathers the impulse and amplifies it, sending it through the BUNDLE OF HIS and into the right and left bundle branches. The electrical impulse gathers STRENGTH as it travels these electrical conduits, culminating in the Purkinje fibers near the base of each ventricle. The impulse then cascades through the myocardial cells of the ventricles, bringing the cells and the ventricles to synchronized contraction. The AV node also can generate a pacing impulse when disease or damage to the heart blocks the SA node's impulse, though the AV node impulse is considerably weaker and can sustain limited cardiac function for only a short time.

For further discussion of the AV node within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also BUNDLE BRANCH; BUNDLE BRANCH BLOCK; CARDIAC CYCLE; ELECTROCARDIOGRAM (ECG); SICK SINUS SYNDROME.

automated external defibrillator (AED) A portable, computerized device to shock a HEART in fibrillation (rapid, useless contractions) into a functional rhythm. AEDs debuted in the 1990s and now are available in many public locations and workplaces. Older models are the size of a small briefcase; newer models are smaller and lighter, with some designed for transport by rescuers on bicycles or on foot. Though manufacturers and emergency medical response experts recommend people obtain training in their use, the devices are simple enough for anyone to use without training. Most models use a computerized voice to provide step-by-step instructions. Once the rescuer applies the pads to the chest of the person having the HEART ATTACK, the AED automatically reads the electrical activity of the heart and determines whether there is sufficient activity for an electrical shock to be therapeutic. An electrical shock cannot help a heart that has no electrical activity. The AED is preset to deliver a precise level and length of shock. AEDs are also available for home use by people at high risk for life-threatening arrhythmias. Many emergency response courses, including the basic life support curriculum, routinely teach AED use.

See also ARRHYTHMIA; CARDIAC ARREST; CARDIOPULMONARY RESUSCITATION (CPR); CARDIOVERSION; ELECTROCARDIOGRAM (ECG); SUDDEN CARDIAC DEATH.

B

blood pressure The force BLOOD exerts against the walls of the arteries as it travels through them, as a combination of resistance and the HEART's pumping effort. A sphygmomanometer is the device that measures blood pressure, reported in millimeters of mercury (mm Hg). A typical blood pressure reading reports the pressure at the peak (systole, at ventricular contraction) and trough (diastole, at ventricular filling) of the CARDIAC CYCLE. The first number in a blood pressure reading is the systolic measure and the second number is the diastolic measure. These measures are independently important as well as significant in combination. Blood pressure is among the vital signs health-care providers measure to assess general health status.

Several mechanisms within the body, including neurologic actions in the brainstem and hormonal actions initiated in the KIDNEYS, regulate blood pressure. Clusters of specialized NERVE cells in the heart and major arteries, called baroreflex sensors, continuously send biochemical signals to the regulatory mechanisms. These mechanisms are redundant—that is, they overlap one another to respond to physiologic changes such as fluid volume and oxygen demand. These mechanisms increase blood pressure by constricting arteries and arterioles, raising the resistance blood encounters as it flows through these blood vessels, and correspondingly increasing the rate and force of the heart's contractions. They decrease blood pressure through reverse actions, dilating arteries and arterioles and decreasing the heart's pumping force. Blood pressure typically increases with exercise or stress, reflecting increased METABOLISM. Higher blood pressure pushes oxygen and NUTRIENTS more rapidly into the CAPILLARY BEDS, speeding the rate at which these substances reach cells.

Blood pressure that is higher than is optimal for cardiovascular health is HYPERTENSION; blood pressure that is too low to adequately circulate blood is HYPOTENSION. Most hypotension occurs as a SIDE EFFECT of medications or neurologic conditions, although some degree of hypotension is common with cardiovascular slowing in aging. Researchers believe age-related hypotension reflects disturbances of the baroreflexes. Cardiologists may prescribe medications to constrict the arteries and intensify the heart's contractions when hypotension causes symptoms such as mental confusion or SYNCOPE (fainting).

BLOOD PRESSURE VALUES

Classification	Systolic	Diastolic
healthy	below 120 mm Hg	below 80 mm Hg
prehypertension	120–139 mm Hg	80–89 mm Hg
stage 1 hypertension	140–159 mm Hg	90–99 mm Hg
stage 2 hypertension	160 mm Hg and above	100 mm Hg and above

Hypertension poses a significant threat to cardiovascular health, raising the risk for HEART ATTACK, RENAL FAILURE, and STROKE. Researchers do not fully understand how hypertension develops, though they do know the contributing factors the development of it (salt intake, physical inactivity, OBESITY, and DIABETES) as well as how to influence blood pressure regulatory mechanisms to bring it under control in most situations. Hypertension exists when either systolic or diastolic pressure is elevated. Health conditions that contribute to hypertension include

- arteriosclerosis, atherosclerotic disease, and cigarette smoking, each of which stiffens the arteries and narrows the arterioles

- diabetes, which damages the blood vessels, particularly the smaller arteries and the arterioles
- OBESITY, which increases body mass and creates additional pressure against the blood vessels

Health experts recommend reduced salt consumption, WEIGHT LOSS AND WEIGHT MANAGEMENT, daily physical exercise, and no smoking to maintain optimal blood pressure. Many people who have hypertension also are on ASPIRIN THERAPY or ANTICOAGULATION THERAPY to reduce their risk for heart attack and stroke.

See also ARTERY; EXERCISE AND HEALTH; LIFESTYLE AND CARDIOVASCULAR HEALTH.

body shape and cardiovascular health Although OBESITY in general raises the risk for numerous health conditions, the distribution pattern of excess body fat correlates to the level of risk for CARDIOVASCULAR DISEASE (CVD) as well as other health conditions such as DIABETES. Numerous research studies affirm that people who carry excess body fat primarily around the waist, the "apple" or "fat tire" body shape, are three times more likely to develop cardiovascular conditions such as HYPERTENSION (high BLOOD PRESSURE), ATHEROSCLEROSIS, CORONARY ARTERY DISEASE (CAD), ISCHEMIC HEART DISEASE (IHD), and PERIPHERAL VASCULAR DISEASE (PVD).

WAIST AND HIP MEASUREMENTS

To measure the waist:

1. Breathe out.
2. Place a measuring tape (or piece of string) snugly but not cinched around the waist, between the crest of the hip bones and the navel (belly button).
3. Note the measurement (or use a ruler to measure the string).

To measure the hips:

1. Place a measuring tape (or piece of string) snugly but not cinched around the hips at their widest point.
2. Note the measurement (or use a ruler to measure the string).

Researchers believe the "apple" pattern of body fat distribution reflects a higher level of INSULIN RESISTANCE than the "pear" body shape in which the body stores excess fat in the hips, thighs, and more equitably throughout the body. This is significant because INSULIN plays a key role in LIPID METABOLISM and regulating blood levels of cholesterol and triglycerides. Excesses of these lipids (HYPERLIPIDEMIA) lead to atherosclerosis, the accumulation of deposits in the inner layer of the walls of the arteries. Atherosclerosis is the foundation of occlusive cardiovascular conditions such as CAD and PVD, and the cause of some types of hypertension (namely renal vascular hypertension).

The WAIST-TO-HIP RATIO (WHR), which is the WAIST CIRCUMFERENCE divided by the hip circumference, determines a person's body shape classification. A WHR greater than 0.9 in men or 0.8 in women defines a body shape as "apple." Maintaining a healthy weight and daily physical exercise are especially important for people who have "apple" body shapes. Exercise improves INSULIN sensitivity and helps keep blood lipid levels and blood pressure within healthy ranges. In turn, this reduces the risk for diabetes as well as cardiovascular disease.

See also ABDOMINAL ADIPOSITY; EXERCISE AND HEALTH; LIFESTYLE AND CARDIOVASCULAR HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

bundle branch An organization of NERVE fibers along the heart's ventricular septum that conveys electrical impulses to the ventricles to cause them to contract, also called the BUNDLE OF HIS. The right bundle branch extends to the right ventricle and the left bundle branch to the left ventricle. The electrical impulses, which originate with the SINOATRIAL (SA) NODE, intensify as they travel along the bundle branches. The bundle branches, as the name implies, branch out into smaller and smaller fibers culminating in the Purkinje fibers, which disperse the electrical impulses to the myocardial cells throughout the ventricles.

For further discussion of the bundle branches within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also ATRIOVENTRICULAR (AV) NODE; BUNDLE BRANCH BLOCK; ELECTROCARDIOGRAM (ECG); HEART.

bundle branch block An impediment, partial or complete, that prevents electrical impulses from

traveling along the BUNDLE OF HIS or one of the bundle branches, right or left, in the HEART. The bundle branches focus and intensify the pacing signals that originate in the SINOATRIAL (SA) NODE, concentrating them enough to stimulate and synchronize the powerful contractions the ventricles need to eject BLOOD from the heart. Various factors can block this electrical pathway. Among the most common are CORONARY ARTERY DISEASE (CAD), VALVULAR HEART DISEASE, HEART FAILURE, and CARDIOMYOPATHY. These conditions result in abnormal blood supply to the myocardial cells, interfering with their normal functions. BUNDLE BRANCH block also can exist without an identifiable cause in people who have no apparent heart disease.

Bundle branch block typically shows up on an ELECTROCARDIOGRAM (ECG) though often does not cause symptoms. The heart continues to contract and pump blood normally (unless other heart disease interferes) because factors other than electrical stimulation contribute to heart function. However, the slowed, delayed, or interrupted flow of the electrical pacing impulse can cause a slow heart rate (bradycardia) or other types of ARRHYTHMIA. The location of the blockage can disrupt the synchronized contractions of the ventricles, causing one to contract before the other instead of both contracting simultaneously. Often, the bundle branch block requires only regular monitoring, not treatment. The location and extent of the block determines the approach. When the block is fairly extensive, a PACEMAKER may be necessary to regulate the heart's electrical activity. Bundle branch block that coexists with other forms of heart disease may require careful coordination of therapeutic measures to preserve overall cardiac function to the greatest extent possible.

See also SICK SINUS SYNDROME.

bundle of His The bundle of NERVE fibers that conveys the heart's electrical pacing impulse from the ATRIOVENTRICULAR (AV) NODE to the ventricles, also called the bundle branches. The short trunk portion of the bundle before it splits into the right BUNDLE BRANCH (right bundle of His) and left bundle branch (left bundle of His) is the main bundle of His. The German physician Wilhelm His (1863–1934) discovered the bundle branches in 1893. Doctors may use the terms bundle of His and bundle branch interchangeably.

For further discussion of the bundle of His within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also ARRHYTHMIA; BUNDLE BRANCH BLOCK; HEART; SICK SINUS SYNDROME.

C

capillary beds The meshlike network of arterioles and venules, the body's tiniest BLOOD vessels, where OXYGEN–CARBON DIOXIDE EXCHANGE takes place. Arterial pressure forces blood into the capillary beds. Erythrocytes (red blood cells) carry oxygen and other NUTRIENTS to the capillary beds, where these molecules pass through to cells. Correspondingly, the cells pass metabolic waste such as CARBON DIOXIDE and lactic acid through to the blood. The arterioles and the venules intertwine in the capillary beds, becoming indistinguishable. Capillary beds are present throughout the body.

For further discussion of the capillary beds within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also ARTERY; ERYTHROCYTE; LUNGS; VEIN.

cardiac arrest Cessation of the heart's contractions. Cardiac arrest may occur as the result of arrhythmias (irregularities in the heartbeat), MYOCARDIAL INFARCTION (clot that blocks the flow of BLOOD through the CORONARY ARTERIES to the HEART MUSCLE), HYPOXIA (such as in drowning), ELECTROCUTION, COCAINE use, or blunt trauma to the chest. Without immediate resuscitative efforts to restore heartbeat, OXYGENATION, and circulation, death occurs within minutes. About 350,000 Americans die of cardiac arrest each year.

Although cardiac arrest can follow HEART ATTACK, they are not the same event. Cardiac arrest typically occurs suddenly and with few warning indications. People at highest risk for cardiac arrest are those who have disorders of the heart's electrical system such as LONG QT SYNDROME (LQTS), SICK SINUS SYNDROME, BUNDLE BRANCH BLOCK, WOLFF-PARKINSON-WHITE SYNDROME, and ventricular arrhythmias.

More than half of cardiac arrests occur in people who do not know they have CARDIOVASCULAR DISEASE. Most cardiac arrests take place at home with no one witnessing the event. By the time someone finds the person who has had cardiac arrest, often it is too late for resuscitation to succeed. Health experts believe prompt resuscitation could save 70 to 80 percent of people who experience cardiac arrest. CARDIOPULMONARY RESUSCITATION (CPR) is most effective within four minutes of the onset of cardiac arrest. Automated external defibrillators (AEDs), small computerized devices that automatically read the heart's rhythm and can administer a jolt of electricity to shock the heart into a functional rhythm, have become more common in public locations and at workplaces. AEDs have saved numerous lives of people who have had cardiac arrests.

See also ARRHYTHMIA; AUTOMATED EXTERNAL DEFIBRILLATOR (AED); CARDIOPULMONARY RESUSCITATION (CPR); SUDDEN CARDIAC DEATH.

cardiac capacity The ability of the HEART to increase CARDIAC OUTPUT to meet the body's increased needs for oxygen during physical activity or exercise. Cardiac capacity is a combination of the heart's physical condition and the body's AEROBIC FITNESS level. Damage to the heart, such as may occur with MYOCARDIAL INFARCTION and ISCHEMIC HEART DISEASE (IHD), reduces cardiac capacity, as do conditions that weaken the heart MUSCLE such as CARDIOMYOPATHY and HEART FAILURE. Cardiac capacity also diminishes as a normal dimension of aging. Aerobic conditioning through consistent, moderate to intense, AEROBIC EXERCISE improves cardiac capacity and helps sustain cardiovascular health.

See also AEROBIC CAPACITY; AEROBIC EXERCISE; AGING, CARDIOVASCULAR CHANGES THAT OCCUR WITH; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH.

cardiac catheterization A diagnostic or therapeutic procedure in which the cardiologist inserts a long, flexible, thin tube into an ARTERY near the surface of the SKIN and threads it through the artery into the HEART or the CORONARY ARTERIES. The cardiologist uses FLUOROSCOPY (moving X-RAY) to view the progress of the catheter's insertion via closed-circuit television. During cardiac catheterization the cardiologist typically injects dye into the coronary arteries to visualize the flow of BLOOD through them (cardiac ANGIOGRAM).

Reasons for Doing This Test

Cardiac catheterization helps diagnose CORONARY ARTERY DISEASE (CAD) and the extent of coronary artery occlusion (blockage). The cardiologist also may use cardiac catheterization to diagnose damaged or dysfunctional heart valves and biopsy the endomyocardium (inner lining and MYOCARDIUM of the heart). Therapeutic applications of cardiac catheterization include ATHERECTOMY and percutaneous transluminal coronary angioplasty (PCTA), also called balloon ANGIOPLASTY. In PCTA the cardiologist inflates a tiny balloon at the catheter's tip to compress ATHEROSCLEROTIC PLAQUE that is occluding a coronary artery.

Preparation, Procedure, and Recovery

Cardiac catheterization requires little preparation beyond nothing to eat or drink for six to eight hours before the scheduled procedure. The catheterization takes place in a sterile setting. Because there is a slight risk for complications that would require immediate OPEN HEART SURGERY, the catheterization facility has full operating room and surgical team capacity. At the start of the procedure the cardiologist administers a general sedative to help the person relax, and injects a local anesthetic into the tissues around the area where the catheter will enter the artery. The cardiologist makes a tiny incision to gain entrance to the artery, and threads the catheter through the artery to the heart and coronary arteries. Typically the cardiologist videotapes the catheterization for further study or review following the procedure.

Depending on the reason for the catheterization and the cardiologist's findings, the procedure takes 45 to 90 minutes. When finished, the cardiologist withdraws the catheter, sutures the insertion incision, and places a pressure dressing over the wound. The person remains lying down for six to eight hours, in a recovery area, allowing a good clot formation to develop and also permitting the sedative to wear off. Most people are able to go home the same day, though must have a friend or relative do the driving, and can return to regular activities within a week.

Risks and Complications

The most significant, though an uncommon, risk of cardiac catheterization is HEART ATTACK or STROKE from atherosclerotic plaque the catheter dislodges. Some people may have a HYPERSENSITIVITY REACTION or allergic response to the injected dye with angiogram. Also uncommon—though possible—is that the cardiologist may discover, upon reaching the occlusion, that the atheroma (plaque formation) is unstable and may determine that immediate CORONARY ARTERY BYPASS GRAFT (CABG) will be necessary. More common complications include bleeding and discomfort at the insertion site or INFECTION after the procedure. For most people, cardiac catheterization is uneventful and provides the information the cardiologist needs to make a definitive diagnosis.

See also STENT; SURGERY BENEFIT AND RISK ASSESSMENT; VALVULAR HEART DISEASE.

cardiac cycle The complete sequence of the heart's contractions that results in ejecting BLOOD from the HEART to the LUNGS and body. Each cardiac cycle represents two paired actions that begin when the SINOATRIAL (SA) NODE, a cluster of specialized NERVE cells located at the apex of the right atrium, emits an electrical pacing impulse. The impulse causes the right and left atria to contract simultaneously, sending blood to the respective ventricles. The right atrium sends to the right ventricle deoxygenated blood returning to the heart from the body; the left atrium sends to the left ventricle oxygenated blood returning to the heart from the lungs.

The ATRIOVENTRICULAR (AV) NODE, a second cluster of specialized nerve cells located at the base of

the right atrium, initiates the second phase of the cardiac cycle. The AV node picks up, amplifies, and focuses the electrical impulse that has passed through the atria, sending it along the BUNDLE OF HIS and the bundle branches in wavelike fashion. The impulse causes the ventricles to contract simultaneously. The right ventricle pumps blood to the lungs for OXYGENATION, and the left ventricle pumps oxygenated blood into the AORTA for the arterial network to carry through the body.

The PULSE represents a completed cardiac cycle. The heart of an adult at rest completes about 80 cardiac cycles each minute. ARRHYTHMIA, VALVULAR HEART DISEASE, CORONARY ARTERY DISEASE (CAD), ISCHEMIC HEART DISEASE (IHD), congenital defects of the heart, and damage to the heart such as occurs with HEART FAILURE or HEART ATTACK are among the conditions that can disrupt the cardiac cycle.

See also BLOOD PRESSURE; BUNDLE BRANCH; CONGENITAL HEART DISEASE; SICK SINUS SYNDROME.

cardiac enzymes Proteins the HEART releases into the bloodstream when HEART ATTACK or other circumstances cause damage to the heart MUSCLE (MYOCARDIUM). BLOOD tests that measure the levels of these enzymes help doctors determine whether, and how long ago, a heart attack has taken place. All muscle tissue releases certain enzymes when injured, so the combination of enzymes present in the blood provides the most useful clues as to the source of the injury. The cardiac-specific enzymes that indicate heart attack are cardiac troponin-T and cardiac troponin-I. The levels of these enzymes in the blood rise 3 to 6 hours after damage to the heart and remain elevated for 7 to 10 days.

Nonspecific enzymes that may suggest heart attack include creatine kinase (CK), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH). Elevations of these enzymes occur whenever there is significant damage to muscle tissue of any kind. To cardiologists determining whether a person has had a heart attack, it is the rise and fall of the enzyme levels that are more useful than the levels themselves at any one point in time. Creatine kinase MB (CK-MB), one of the protein components of creatine kinase, rises more rapidly and dramatically when the damage is to heart muscle, providing a strongly suggestive marker. CK-MB rises within a few hours of heart damage though returns to normal in about 24 hours. Cardiologists evaluate cardiac enzyme levels in combination with other clinical evidence such as ELECTROCARDIOGRAM (ECG) and ECHOCARDIOGRAM to confirm the diagnosis of MYOCARDIAL INFARCTION (death of heart muscle cells due to lack of oxygen).

See also CARDIAC CATHETERIZATION.

cardiac intensive care unit (CICU) A specialized unit within a hospital that provides comprehensive medical care for people recovering from HEART ATTACK or receiving treatment for other life-threatening cardiovascular diseases. Large hospitals have separate units for medical patients (such as those who have had HEART attacks but not surgery) and surgical patients (such as those who have had CORONARY ARTERY BYPASS GRAFT (CABG), heart valve replacement, or other operations on the heart); in smaller hospitals a single specialized unit provides care for both kinds of patients. The nurses and ancillary health-care staff who work in CICUs have specialized training in using the monitoring equipment and caring for patients who have serious cardiovascular conditions. Most CICUs restrict visitors and visiting times to protect patients and allow them to receive adequate rest as well as the intensive nursing care their conditions require.

See also CARDIAC REHABILITATION; HEART TRANSPLANTATION; MECHANICAL VENTILATION.

cardiac output The volume of BLOOD the HEART pumps out to the body each minute. Cardiac output is an important measure of the heart's efficiency. Many cardiovascular diseases, such as ARRHYTHMIA and HEART FAILURE, can limit cardiac output. Cardiologists measure cardiac output as the combination of HEART RATE and stroke volume (the amount of blood the left ventricle ejects into the AORTA with each contraction). There are several methods for determining stroke volume, including dye injection and thermal differential.

In a person whose cardiovascular system is healthy, cardiac output increases with increased physical activity such as exercise, in which both heart rate and the force of the heart's contractions increase. A heart with damage due to disease such as CARDIOMYOPATHY or HEART FAILURE, or as a conse-

quence of MYOCARDIAL INFARCTION, cannot increase the force of its contractions, limiting cardiac output. Severe damage can result in cardiac output that is less than the body's needs even at rest. Medications to strengthen the heart and focus the efforts of its contractions can often improve cardiac efficiency, though only mediating the underlying cause can restore adequate cardiac output.

People who have a high AEROBIC FITNESS level, such as athletes and those who regularly engage in AEROBIC EXERCISE, can significantly increase their cardiac output to send more blood to their muscles. During intense aerobic activity, 60 percent or more of the cardiac output may go to the skeletal muscles. High cardiac output is essential to get enough blood and oxygen to vital organs at the same time.

See also CARDIAC CAPACITY; LEFT VENTRICULAR EJECTION FRACTION (LVEF).

cardiac rehabilitation Planned activities, course of recovery, or structured program for improving cardiovascular health after HEART ATTACK, CORONARY ARTERY BYPASS GRAFT (CABG), HEART TRANSPLANTATION, and other major cardiovascular events or operations. Many people, after such events, need to make significant lifestyle changes. A structured cardiac rehabilitation program helps people to define their needs and goals and establish realistic steps to move progressively toward meeting them. Most people benefit from assistance with meal planning and nutrition, exercise, and SMOKING CESSATION. Structured programs also offer social interaction with other people who have similar experiences, and may include organized SUPPORT GROUPS for people to share their feelings, perceptions, and suggestions.

Many factors influence a person's ability to participate in physical activity. Many hospitals and medical centers offer physician-supervised cardiac rehabilitation programs that feature defined yet individualized activities, some of which may take place at a facility such as a rehabilitation center and others designed for the person to do at home. Some medically supervised cardiac rehabilitation programs incorporate ambulatory ELECTROCARDIOGRAM (ECG) so people can use the telephone to send their ECG readings to cardiologists who can then determine whether physical exercise is within therapeutic range and provide assurance that the HEART is functioning satisfactorily.

Programs such as those health clubs and organizations such as the YMCA offer are less comprehensive and not under a physician's direction. They primarily provide classes in aerobic and resistance exercises as well as access to facilities and equipment. A nutritional counselor separately provides dietary guidance including instruction for WEIGHT LOSS AND WEIGHT MANAGEMENT. People who have health conditions other than cardiovascular, such as DIABETES or chronic OSTEOARTHRITIS, may need additional consultations or professional guidance to accommodate all of their health needs.

Current medical practice emphasizes a return to regular activities as quickly as possible following heart attack or major heart surgery. This reduces the risk of BLOOD clots that can cause STROKE, another heart attack, or PULMONARY EMBOLISM (blood clot in the LUNG). It also expedites HEALING and counters the emotional swings, especially DEPRESSION and anxiety, that are common with serious CARDIOVASCULAR DISEASE (CVD). Research studies have conclusively demonstrated that people who engage in cardiac rehabilitation and maintain heart-healthy lifestyle changes are much less likely to experience additional cardiovascular events and may even halt or reverse cardiovascular conditions such as ATHEROSCLEROSIS and HYPERTENSION (high BLOOD PRESSURE).

BENEFITS OF CARDIAC REHABILITATION

decreased CHOLESTEROL BLOOD LEVELS	faster return to work and other activities
fewer cardiovascular symptoms	improved AEROBIC FITNESS
improved ATHEROSCLEROSIS	improved INSULIN sensitivity
improved nutritious eating habits	improved QUALITY OF LIFE
lowered BLOOD PRESSURE	reduced postoperative discomfort
reduced risk of health problems related to smoking	stress reduction

WEIGHT LOSS AND WEIGHT MANAGEMENT

Heart attack or major heart surgery is a significant trauma for an individual to experience, with both physical and emotional components. Many people are fearful about the level of physical activity their bodies, and especially hearts, can tolerate. Some people respond with reluctance to do anything and others leap into action with a fervor

that would challenge even someone in peak cardiovascular function. Neither extreme is healthy and can result in further health problems. A person who has not been physically active for years to decades often benefits from the advice and suggestions of a health expert who can help determine an appropriate entry point for returning to an active lifestyle.

Recent studies affirm that cardiac rehabilitation has therapeutic value for people who have chronic cardiovascular conditions such as congestive HEART FAILURE, improving symptoms and QUALITY OF LIFE. Many people will begin cardiac rehabilitation before leaving the hospital after treatment or surgery, starting with an exercise STRESS TEST to determine cardiopulmonary capacity, and continue in a structured way for 3 to 6 months. Under ideal circumstances the activities of rehabilitation, including EATING HABITS and nutrition, become elements of routine daily living and foster a lifestyle that supports cardiovascular health.

See also DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND CARDIOVASCULAR HEALTH; NUTRITIONAL ASSESSMENT; NUTRITIONAL NEEDS; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; SEXUAL ACTIVITY AND CARDIOVASCULAR DISEASE.

cardiac resynchronization therapy (CRT) A method of biventricular pacing in which an implanted device regulates and coordinates the contractions of both ventricles, typically to treat severe HEART FAILURE. SUDDEN CARDIAC DEATH as a result of ARRHYTHMIA is a significant risk in HEART failure, particularly heart failure resulting from dilated CARDIOMYOPATHY. Certain BUNDLE BRANCH BLOCK arrhythmias also benefit from CRT.

Conventional pacing therapy stimulates only the right ventricle, which in an otherwise healthy heart results in contraction of both ventricles as the electrical impulse spreads simultaneously across them. In severe heart failure, however, both ventricles are extensively damaged and do not function in synchronization. Conventional pacing therapy ends up being counterproductive by further extending the dysfunction between the two ventricles. A biventricular PACEMAKER has two leads (wires that conduct electrical impulses), one of which the cardiologist inserts in each ventricle. The pacemaker's discharge sends impulses simultaneously to each lead.

The risks of CRT are similar to those of conventional pacing therapy and include possible INFECTION or blood clots from the inserted leads. These risks are minimal, however, and CRT provides substantial benefit for people whose arrhythmias due to heart failure do not respond to other treatments.

See also IMPLANTABLE CARDIOVERTER DEFIBRILLATOR.

cardiomyopathy Weakness and loss of pumping effectiveness of the HEART, usually with changes to the structure of the heart and in particular the left ventricle. Cardiomyopathy is as likely to affect people under age 40 as people over age 60 and is a leading cause of HEART FAILURE resulting in HEART TRANSPLANTATION. Genetic factors can play a role in cardiomyopathy, especially in younger people, though lifestyle factors such as nutrition and ALCOHOL consumption are also significant. Viral and bacterial infections of the heart (MYOCARDITITIS) can leave the heart MUSCLE damaged. In many situations, however, doctors do not know what causes the structural and functional changes in myocardial (heart muscle) cells that result in primary cardiomyopathy. Secondary cardiomyopathy may also develop as a consequence of other CARDIOVASCULAR DISEASE (CVD), such as ISCHEMIC HEART DISEASE (IHD) and HYPERTENSION (high BLOOD PRESSURE).

The five major types of cardiomyopathy are

- **Dilated cardiomyopathy,** in which the heart enlarges in an attempt to compensate for damage to myocardial cells that limits the heart's ability to efficiently pump BLOOD. Long-term ALCOHOL abuse accounts for the dilated cardiomyopathy in about a third of the people who develop it. Deficiency of vitamin B_1 also damages the heart. Though uncommon in the general US population, vitamin B_1 deficiency can occur with long-term, heavy alcohol consumption as well as with long-term EATING DISORDERS such as anorexia nervosa. Dilated cardiomyopathy is more common in people over age 60.
- **Hypertrophic cardiomyopathy,** in which the walls of the heart, particularly the ventricles, thicken. Some doctors may refer to this

condition as hypertrophic obstructive cardiomyopathy (HOCM) or idiopathic hypertrophic subaortic stenosis (IHSS), both of which are older terms. Hypertrophic cardiomyopathy is hereditary, the result of mutations in a number of genes that regulate proteins essential for myocardial cell contractions (notably myosin, troponin T, and alpha tropomyosin). The hypertrophy, or thickening, typically affects the left ventricle most extensively and can involve the ventricular septum to the extent that the hypertrophy creates an obstruction for the proper functioning of the aortic valve (AORTIC STENOSIS). Undiagnosed hypertrophic cardiomyopathy is a leading cause of SUDDEN CARDIAC DEATH in younger people, especially athletes.

- **Ischemic cardiomyopathy,** which develops secondary to longstanding IHD or following extensive or repeated MYOCARDIAL INFARCTION. Ischemia results from inadequate oxygen supply to the cells, some of which die. The patches of dead muscle tissue do not contract, diminishing the heart's effectiveness. Ischemic cardiomyopathy is more common in people over age 60 who have other forms of cardiovascular disease.
- **Peripartum cardiomyopathy,** which develops in a woman during late PREGNANCY or in the first few months after CHILDBIRTH. It appears an inflammatory process in the body, though doctors are uncertain what sets it off. In some situations there is a clear bacterial or viral INFECTION, but most often there is no apparent reason for the INFLAMMATION. Most women fully recover from peripartum cardiomyopathy though are at increased risk for developing it again with subsequent pregnancies.
- **Restrictive cardiomyopathy,** in which the myocardial cells accumulate deposits that cause them to lose elasticity. The loss restricts the ability of the heart to expand, reducing the ability of the ventricles to properly fill with blood. As a consequence, the heart cannot pump enough blood to meet the body's needs. Restrictive cardiomyopathy is secondary to other health conditions such as AMYLOIDOSIS, which leaves protein deposits, and HEMACHROMATOSIS, which leaves iron deposits.

Symptoms and Diagnostic Path

Cardiomyopathy often does not show symptoms until the condition is quite advanced, and then the symptoms are likely to be those of other cardiovascular conditions, such as hypertension and heart failure, especially congestive heart failure. Doctors commonly discover cardiomyopathy during chest X-RAY done for other reasons. When symptoms are present, they typically include

- shortness of breath (DYSPNEA)
- weakness and tiredness
- inability to participate in physical activities

The diagnostic path includes ELECTROCARDIOGRAM (ECG), which detects the arrhythmias typical of an overworked heart, and ECHOCARDIOGRAM, which shows the heart's enlargement and altered function. These tests can provide definitive diagnosis for most cardiomyopathy. Other diagnostic procedures the cardiologist may recommend, depending on the kind of cardiomyopathy suspected, may include COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), transesophageal echocardiogram (TEE), angiogram, and myocardial biopsy. GENETIC TESTING to detect mutations commonly associated with hypertrophic cardiomyopathy can help detect the potential for this condition before it manifests symptoms, allowing prophylactic interventions to delay or minimize its development.

Treatment Options and Outlook

All forms of cardiomyopathy make it difficult for the heart to pump blood effectively. Though in the early stages of the condition the heart's enlargement can compensate for some of the diminished STRENGTH, eventually the compensatory measures become ineffective and even counterproductive. Treatment targets improving the heart's efficiency, usually through a combination of medications and lifestyle modifications. Medications typically include diuretics to reduce edema (fluid accumulations), antiarrhythmia medications to maintain the heart's regular rhythm, vasodilator medications to relax the blood vessels and reduce resistance for blood flow, and medications such as digoxin (inotropic medications) to strengthen the heart's pumping effectiveness. It also is crucial to

treat any coexisting or causative cardiovascular disease such as hypertension, ATHEROSCLEROSIS, and CORONARY ARTERY DISEASE (CAD). Such measures allow the majority of people who have cardiomyopathy, particularly dilative cardiomyopathy, to enjoy normal lives.

Progressive cardiomyopathy necessitates substantial lifestyle changes and is a leading cause of disability due to cardiovascular disease. Hypertrophic, ischemic, and restrictive cardiomyopathies are most likely to be progressive. The therapeutic approach is to manage symptoms to the extent possible, making lifestyle adaptations such as reduced physical activity to accommodate diminished CARDIAC CAPACITY. Heart transplantation becomes a treatment option for people under age 65 who are otherwise healthy. Cardiomyopathy accounts for about half of heart transplantations performed in the United States. In some situations an implanted ventricular assist device (VAD) can supplement the natural heart's function, allowing the heart to regain strength and recover from damage. A VAD also can serve as a "bridge" to support the heart while a person waits for a donor heart for transplantation. Sometimes other surgical approaches, such as removing a segment of diseased heart tissue to reduce the size of the ventricle, are successful in restoring the heart's functional ability.

Risk Factors and Preventive Measures

The leading risk factors for most forms of cardiomyopathy are physical inactivity and suboptimal nutrition, which are risk factors for cardiovascular disease in general, as well as excessive alcohol consumption, genetics, and other cardiovascular disease. As with any form of cardiovascular disease, controlling lifestyle factors reduces the risk for the condition. Early GENETIC TESTING can help people who have family history of hypertrophic cardiomyopathy to determine whether they are at risk for this condition and to plan appropriate therapeutic approaches to delay its development. Most people who die suddenly because of hypertrophic cardiomyopathy do not know they have the condition. Keeping chronic cardiovascular conditions such as hypertension and atherosclerosis under control reduces the risk for secondary cardiomyopathy.

See also ALCOHOLISM; ARRHYTHMIA; BACTERIA; CARDIOVASCULAR DISEASE PREVENTION; CONGENITAL HEART DISEASE; LIFESTYLE AND CARDIOVASCULAR HEALTH; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; MUTATION; QUALITY OF LIFE; RISK FACTORS FOR CARDIOVASCULAR DISEASE; VENTRICULAR ASSIST DEVICES (VADS); VIRUS.

cardiopulmonary bypass A procedure in which a machine takes over the oxygenation and pumping functions of the LUNGS and HEART, making OPEN HEART SURGERY possible. Cardiopulmonary bypass allows the cardiovascular surgeon to stop the heart to operate on it, using the bypass machine to circulate the BLOOD through the body. Physician and researcher John H. Gibbon Jr. developed the first cardiopulmonary bypass machine during more than two decades of research and experimentation that culminated in its use to repair a congenital malformation in an 18-year-old woman's heart in 1953. Gibbon's design remains the foundation of cardiopulmonary bypass machines in use today.

In cardiopulmonary bypass, the surgeon inserts large catheters (cannulas) into the VENA CAVA and the AORTA, then administers a chemical solution to cause the heart to stop beating (cardioplegia). The cannulas channel blood through the bypass machine, which uses a membrane oxygenator to infuse the blood with oxygen and allow carbon dioxide to diffuse. Large doses of heparin, an anticoagulant medication, keep the blood from clotting, and special filters capture air bubbles. A pump mechanism, commonly roller pumps or centrifugal force, moves the blood through the bypass machine and in circulation through the person's body. The bypass machine also cools the blood during surgery, to reduce oxygen consumption by maintaining the body's METABOLISM at a lower rate, and warms it at the conclusion of surgery to prepare for returning the body to its own cardiovascular circulation. At the conclusion of the OPERATION the surgeon withdraws the cannulas and restores the flow of blood and the heartbeat.

The primary risks of cardiopulmonary bypass are blood clots and air bubbles that can cause embolism (occlusion of a blood vessel), damage to red blood cells (HEMOLYSIS), and systemic inflammatory response (IMMUNE SYSTEM activation). There is much debate about whether microemboli that

slip through filtration can cause damage to the BRAIN and lungs. Some people experience neurologic effects such as cognitive dysfunction, memory difficulties, and mood swings in the months after cardiopulmonary bypass. Cardiopulmonary bypass also can affect lung function. However, for most people the benefit of the operation cardiopulmonary bypass makes possible outweighs the potential risk for these usually transitory side effects. Cardiovascular surgeons continue to explore new techniques that reduce or eliminate the need for cardiopulmonary bypass, including MINIMALLY INVASIVE SURGERY and off-pump procedures though these, too, carry risks.

See also CONGENITAL HEART DISEASE; SURGERY BENEFIT AND RISK ASSESSMENT.

cardiovascular disease (CVD) The collective term for the numerous health conditions of the HEART and BLOOD vessels. Cardiovascular disease (CVD) is the leading cause of death and disability in the United States and in many other developed countries. More than 70 million Americans live with CVD; 10 million of them have sufficient disability that they cannot work or participate in the activities they enjoy. CVD claims over 900,000 lives each year. The most common forms of CVD are HYPERTENSION (high BLOOD PRESSURE), ATHEROSCLEROSIS (occluded arteries), CORONARY ARTERY DISEASE (CAD), and ISCHEMIC HEART DISEASE (IHD). Health experts sometimes refer to CAD and IHD collectively as coronary heart disease (CHD).

Most CVD develops as a consequence of lifestyle factors, though age, gender, and genetic predisposition also contribute. The primary risk factors for CVD are

- cigarette smoking
- OBESITY
- physical inactivity
- DIABETES
- renal (kidney) disease
- being a man under age 50
- age over 50 for men and over 60 for women
- family history of CVD

Acquired CVD is largely preventable through lifestyle practices that incorporate nutritious eating habits, daily physical exercise, and not smoking. These practices are also preventive for health conditions that lead to CVD, such as diabetes and obesity. Other forms of CVD may be hereditary or congenital. Hereditary CVD conditions are the result of GENE mutations. CONGENITAL HEART DISEASE results from structural defects in the heart and its major vessels, such as tetralogy of Fallot, or to blood vessels elsewhere in the body, such as ARTERIOVENOUS MALFORMATION (AVM), that occur during early gestational development and are present at birth.

For further discussion of CVD please see the overview section "The Cardiovascular System."

See also AGING, CARDIOVASCULAR CHANGES THAT OCCUR WITH; LIFESTYLE AND CARDIOVASCULAR HEALTH; PREVENTING CARDIOVASCULAR DISEASE; SMOKING AND CARDIOVASCULAR DISEASE.

cardioversion The application of an electrical shock through the chest wall to the HEART, administered under sedation, to alter the heart's electrical rhythm. The cardiologist performs cardioversion in a hospital setting staffed and equipped to respond to cardiovascular emergencies. There is a slight risk for HEART ATTACK or STROKE. Cardioversion is most commonly a treatment for ARRHYTHMIA such as ATRIAL FIBRILLATION, in which the heart's electrical patterns have gotten out of synchronization in some way. The effect may be permanent, long-lasting, or short term. Some people experience slight SKIN irritation at the site of the electrodes or paddles on the surface of the chest following cardioversion. Because the procedure requires a general sedative, there may also be grogginess for several hours. Most people go home within 4 to 6 hours and return to their usual activities the following day.

See also DEFIBRILLATION; IMPLANTABLE CONVERTER DEFIBRILLATOR (ICD); RADIOFREQUENCY ABLATION.

carotid bruit An abnormal sound characteristic of ATHEROSCLEROSIS that the cardiologist hears through a STETHOSCOPE placed over the carotid ARTERY at the base of the neck. The sound, a murmur that occurs during systole (contraction of the left ventricle), represents turbulence as BLOOD passes through areas of the carotid artery where atheromas (collections of ATHEROSCLEROTIC PLAQUE)

occlude the inner channel of the carotid artery. Carotid bruit is a diagnostic sign that indicates the presence of CAROTID STENOSIS (narrowing of the carotid artery) and increased risk for STROKE.

See also ANGIOGRAM; ENDARTERECTOMY; HEART SOUNDS; STENT.

carotid stenosis Narrowing of the carotid ARTERY in the neck due to ATHEROSCLEROSIS. Often carotid stenosis shows no symptoms until it results in a STROKE. The doctor may detect carotid stenosis during routine physical examination when listening to the carotid arteries with a STETHOSCOPE, which reveals the characteristic murmur sound, CAROTID BRUIT, that indicates the stenosis. ANTICOAGULATION THERAPY, most commonly ASPIRIN THERAPY, helps reduce the risk of clot formation at the site of the stenosis though does not prevent or reduce atherosclerotic accumulations. ENDARTERECTOMY, surgery to remove the occluding atheromas (collections of ATHEROSCLEROTIC PLAQUE) and widen the arterial passage, becomes a viable treatment option when the stenosis reaches 60 or 70 percent. ANGIOGRAM, in which the cardiologist uses dye and X-rays to examine the arteries, helps define the degree of occlusion. Stroke occurs when clot or atheroma fragments break free from the site of the stenosis and travel through the carotid artery to the BRAIN.

See also CARDIOVASCULAR DISEASE PREVENTION; SURGERY BENEFIT AND RISK ASSESSMENT.

chest pain Discomfort that arises from the upper portion of the body. CHEST PAIN can have various causes, many of which are not cardiovascular. Discomfort originating from the HEART is characteristically oppressive in nature, though often not the crushing pressure that is the common perception. As many as 25 percent of people do not experience appreciable pain with HEART ATTACK. Gastrointestinal pain often sends people to the emergency room worried about heart attack, yet nearly a third of people who are having heart attacks delay seeking medical care because they do not believe the symptoms they are experiencing, especially chest pain, are severe enough to be heart attack. Chest pain is unreliable as an indicator of the nature or severity of a health situation.

HEALTH CONDITIONS THAT CAN CAUSE CHEST PAIN

BARRETT'S ESOPHAGUS	COSTOCHONDRITIS
dissecting aortic ANEURYSM	ENDOCARDITIS
GALLBLADDER DISEASE	GASTROESOPHAGEAL REFLUX DISORDER (GERD)
HEPATIC ABSCESS	HIATAL HERNIA
LUNG ABSCESS	MYOCARDITIS
PANCREATITIS	PEPTIC ULCER DISEASE
PERICARDITIS	PNEUMONIA
PLEURISY	rib FRACTURES
PULMONARY EMBOLISM with infarction	STOMACH CANCER

See also CARDIOPULMONARY RESUSCITATION (CPR); CHONDRITIS; COCAINE.

cholesterol blood levels The amounts and forms of cholesterol that are present in the bloodstream, usually measured after 8 to 12 hours of fasting (no food) to accommodate short-term rises that could result from eating. Cholesterol is a sterol, a chemical essential for numerous metabolic functions and necessary for health. Because cholesterol cannot dissolve in the BLOOD, it binds with protein carriers called lipoproteins that suspend it in the blood. Cholesterol becomes a health problem when the amount of cholesterol in the blood cir-

CHOLESTEROL BLOOD LEVELS AND CARDIOVASCULAR HEALTH

Cholesterol	Optimal	Moderate Risk	High Risk
HDL-C	≥ 60 mg/dL	< 40 mg/dL	not applicable
LDL-C	≤ 100 mg/dL*	130–159 mg/dL*	>160 mg/dL
total cholesterol	< 200 mg/dL	200–239 mg/dL	≥ 240 mg/dL

**For people with no other cardiovascular risk factors, LDL-C levels of 100–129 mg/dL is optimal. For people with other cardiovascular risk factors, LDL-C levels of 100–129 mg/dL is nearly optimal/slight risk.*

culation exceeds the body's needs. The excess lipoproteins that transport the cholesterol fall out of suspension and infiltrate the inner lining of the arterial walls, forming ATHEROSCLEROTIC PLAQUE. Health factors that increase the risk of elevated lipoprotein-cholesterol blood levels include OBESITY, DIABETES, and HYPERTENSION.

The LIVER produces most of the cholesterol in the blood circulation, manufacturing this necessary chemical from saturated fats and other dietary NUTRIENTS. Dietary cholesterol is a minor factor in this process. The liver continues to manufacture cholesterol as long as it receives the ingredients, via ingested nutrients, to do so. Cells throughout the body also can synthesize cholesterol to meet their needs. The body stores some excess cholesterol, along with other fatty acids (notably triglycerides), in adipose tissue throughout the body. The body can then withdraw this cholesterol when liver synthesis slows. However, adipose tissue can hold only so much. Remaining excess cholesterol stays in the bloodstream.

The liver manufactures the lipoproteins that carry cholesterol as well as triglycerides and phospholipids (collectively called fatty acids or lipids). Different lipoproteins transport the kinds of fatty acids. Very low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) transport some cholesterol and most of the triglycerides. It is the excesses of LDL cholesterol (LDL-C) and VLDL cholesterol (VLDL-C) that create increased cardiovascular health risks. These lipoprotein packages settle out of the blood easily, collecting against the inner walls of the arteries. Over time (typically decades) the lipoproteins, along with other cellular debris that gathers, infiltrates the innermost layer of the arterial wall and forms atherosclerotic plaque. This process is the foundation of ATHEROSCLEROSIS.

High-density lipoprotein (HDL) transports primarily cholesterol. It appears that HDL not only carries cholesterol from the liver but also picks up fragments of cholesterol-bearing LDL and VLDL and returns them to the liver, which disassembles them. Lowering the available lipoproteins in the body reduces the excess circulating in the bloodstream and increases the proportion of HDL cholesterol (HDL-C) to LDL-C/VLDL-C. Cells draw the cholesterol they need from the supply in circulation, helping maintain a healthy balance. Generally, the higher a person's total cholesterol, the higher his or her LDL-C levels.

ADDITIONAL CARDIOVASCULAR RISK FACTORS

age 65 or older	CONGENITAL HEART DISEASE
DIABETES	family history of CARDIOVASCULAR DISEASE (CVD)
female past MENOPAUSE	HEART ATTACK
HYPERTENSION	ISCHEMIC HEART DISEASE (IHD)
male, any age	OBESITY
PERIPHERAL VASCULAR DISEASE (PVD)	physically inactive
smoking	STROKE
TRANSIENT ISCHEMIC ATTACK	

When the body's nutrient intake is in balance, the liver uses up the nutrient components available to manufacture cholesterol and lipoproteins, sending into circulation the levels that the body can use. "Optimal" blood cholesterol values identify this balance, or lipid homeostasis, in which there is no increased cardiovascular risk in most people. Researchers have recently determined the LDL level to be the most significant in people who have other RISK FACTORS FOR CARDIOVASCULAR DISEASE.

Current lipid-lowering treatment recommendations emphasize LDL-C blood values; the recom-

CHOLESTEROL-LOWERING MEDICATION RECOMMENDATIONS

LDL-C Level	Risk Factor Profile	Target LDL-C Level
< 100 mg/dL	CVD + 2 or more CVD risk factors	100 mg/dL
130–160 mg/dL	CVD	100 mg/dL
160–190 mg/dL	2 or more CVD risk factors	130 mg/dL
> 190 mg/dL	no CVD or risk factors	160 mg/dL
190–219 mg/dL	male under age 35	160 mg/dL
190–219 mg/dL	female premenopause	160 mg/dL

mended LDL-C level depends on risk factors for CARDIOVASCULAR DISEASE (CVD). The higher the cardiovascular risk, the lower the recommended LDL-C level.

- Treatment may use lifestyle (diet and exercise) modification alone, which is effective for meeting LDL-C target levels for many people whose LDL-C blood values are 100–130 milligrams per deciliter (mg/dL) and who have no more than one additional CVD risk factor.
- For people who already have some form of CVD or who have two or more additional risk factors for CVD, treatment combines lifestyle with lipid-lowering medications.
- People who have very high CVD risk and very high LDL-C values may take two or more medications to bring their LDL-C blood levels to a healthier range.

Some cardiologists advocate driving LDL-C levels even lower, to 70 mg/dL, in people who have severe risk for HEART ATTACK or STROKE, such as those who have already had such a cardiovascular crisis and have numerous risk factors for cardiovascular disease. For most people, reaching the LDL-C target means a decrease of 30 to 40 percent.

See also CARDIOVASCULAR DISEASE PREVENTION; CHOLESTEROL, DIETARY; CHOLESTEROL, ENDOGENOUS; GARLIC; HYPERLIPIDEMIA; LIFESTYLE AND CARDIOVASCULAR HEALTH; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; TRIGLYCERIDE BLOOD LEVEL; TRIGLYCERIDES, DIETARY.

circle of Willis A looped network (anastamosis) of arteries at the base of the BRAIN. Branches of the internal carotid arteries form the front of the circle and branches of the posterior cerebral arteries form the back of the circle, with smaller arteries, collectively called the communicating arteries, branching from them. The circle of Willis is a unique vascular structure in the body that provides an extended safety net of redundancy for the brain's BLOOD supply; the closest analogous configuration is that of the CORONARY ARTERIES which supply the HEART. Even if damage occurs to one or two of the circle of Willis's anastomosed arteries, blood flow to the brain continues. The base of the skull protects this arterial network. The circle of Willis, because of its complexity, varies anatomically among individuals and is a common site for congenital vascular anomalies (malformations of the blood vessels).

For further discussion of the circle of Willis within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also ARTERIOVENOUS MALFORMATION (AVM); ARTERY.

congenital heart disease HEART conditions, including structural anomalies of the heart, that are present from birth. Some forms of congenital heart disease are mild to moderate and require minimal or one-time intervention to correct. Congenital heart malformations are among the most common BIRTH DEFECTS in the United States. Though still the leading cause of infant death due to birth defects, congenital heart malformations no longer mean certain death. Beginning in the 1950s pediatric cardiology pioneers Alfred Blalock (1899–1964), Helen Taussig (1898–1986), and Vivien Thomas (1910–1985) established many of the operations and surgical techniques that remain in use today to create functional BLOOD flow through malformed hearts. Advances in CARDIOPULMONARY BYPASS and refinements in surgical techniques have made relatively normal lives possible for more than a million children with heart defects born since 1970.

Structural deformities that affect the heart's ability to circulate oxygenated blood result in inadequate oxygen reaching the body's tissues and cause CYANOSIS, a bluish tint to the lips, nail beds, mucous membranes, and SKIN. Doctors collectively refer to these conditions as cyanotic heart disease (sometimes called blue baby syndrome). These conditions are nearly always apparent within 48 hours of birth and typically require fairly immediate intervention (usually surgery). Other forms of congenital heart disease, such as LONG QT SYNDROME (LQTS) and hypertrophic CARDIOMYOPATHY, may not manifest until late childhood or adulthood.

Heart defects may occur in isolation or in combination with GENETIC DISORDERS such as DOWN SYNDROME (trisomy 21) and MARFAN SYNDROME. Heart abnormalities often occur in association with

FORMS OF CONGENITAL HEART DISEASE

anomalous pulmonary venous return	aortic coarctation
AORTIC STENOSIS	atrial septal defect (ASD)
atrioventricular (AV) canal defect	bicuspid aortic valve
Eisenmenger's complex	hypoplastic left heart syndrome (HLHS)
LONG QT SYNDROME (LQTS)	patent ductus arteriosus (PDA)
persistent truncus arteriosus	pulmonary atresia
tetralogy of Fallot	transposition of the great arteries (TPA)
tricuspid atresia	ventricular septal defect (VSD)

abnormalities of the skeletal, urinary, and gastrointestinal systems, forming a collection that doctors refer to by the acronym VACTERL: vertebral, anorectal, cardiac, tracheoesophageal, renal, and limb. About 50 percent of infants born with one congenital anomaly among this grouping have at least one other. Researchers believe about 10 percent of congenital heart malformations result from GENE MUTATION or CHROMOSOME abnormalities.

Common forms of congenital heart disease The most common and most easily treatable congenital heart malformations are patent ductus arteriosus (PDA) and septal defects. The ductus arteriosus is an opening between the AORTA and the pulmonary ARTERY in the FETUS that allows fetal circulation to bypass the nonfunctioning LUNGS (the fetus draws oxygen from the mother's blood supply). At birth a sequence of events takes place, initiated with the pressure changes that occur with the infant's first breath, that cause the ductus arteriosus to close. In some infants, especially those born prematurely, the closure does not take place and the ductus arteriosus remains patent, or open. PDA allows oxygenated and deoxygenated blood to mix in the pulmonary artery, with the result that the blood the aorta sends to the body carries only partial oxygenation.

In a septal defect there is an abnormal opening in the septum, or wall, separating the heart's chambers. A septal defect allows blood to move directly between the involved chambers, which disturbs the flow of blood and can result in blood turbulence and pooling as well as reduced OXYGENATION. The most common presentation is atrial septal defect (ASD), in which the opening is between the right and left atria. The opening may be the result of incomplete closure of the foramen ovale, a natural opening between the atria in the fetus that normally closes within 48 hours of birth. ASD may also occur as a malformation of the atrial septum. A ventricular septal defect (VSD) is a malformation of the ventricular septum and results in an opening between the right and left ventricles. A VSD allows oxygenated and deoxygenated blood to mingle, reducing the oxygen content of the blood the left ventricle pumps out to the body.

Atrioventricular (AV) canal defect is a more extensive malformation of the septum in which the atrial septum, the ventricular septum, or the entire septum is missing. The heart becomes essentially a single large chamber with oxygenated and deoxygenated blood mixing freely. Blood going to the body carries insufficient oxygen, and blood going to the lungs is under much higher pressure than the lungs can accommodate. AV canal defect requires surgical repair within the first few months of the infant's life. Though AV canal defect can occur as an isolated malformation it most often occurs in conjunction with Down syndrome, affecting about 25 percent of Down syndrome infants.

Other common congenital heart defects include coarctation of the AORTA (narrowing and irregularities) and malformations of the heart valves such as AORTIC STENOSIS, bicuspid aortic valve, tricuspid atresia, and pulmonary atresia.

Grave malformations of the heart A number of heart malformations are rare, complex, and life-threatening. Their defects are severe and include alterations of the heart's structure that cannot sustain life. They require immediate surgery for survival and usually follow-up operations for further reconstruction. In some cases the only viable long-

term treatment is HEART TRANSPLANTATION. The most frequently occurring of these grave malformations are

- Tetralogy of Fallot, which is a complex of four structural anomalies: VSD, pulmonary artery and valve malformation, aortic displacement (the aorta arises between the ventricles rather than solely from the left ventricle), and hypertrophic left ventricle (thickening of the left ventricle's wall).
- Transposition of the great arteries (TGA), in which the aorta and the pulmonary artery are switched. The aorta arises from the right ventricle instead of the left, carrying the deoxygenated blood from the right ventricle out to the body. The pulmonary artery arises from the left ventricle instead of the right, taking oxygenated blood back to the lungs from the left ventricle.
- Hypoplastic (or hypotrophic) left heart syndrome (HLHS), in which the left ventricle or the entire left heart fails to develop, resulting in essentially a two-chamber heart. The aorta is usually small or deformed. Blood in the heart is a mix of oxygenated and deoxygenated, and the right ventricle pumps to both the lungs and the body.
- Persistent truncus arteriosus, which is a combination of VSD and deformities of the PULMONARY ARTERIES and aorta that disrupts the heart's ability to pump oxygenated blood to the body.
- Anomalous pulmonary venous return, in which the PULMONARY VEINS attach to the right atrium instead of the left atrium, returning oxygenated blood to the same chamber that pumps deoxygenated blood to the lungs. This malformation typically occurs in combination with ASD, so the flow of blood between the atria moves some oxygenated blood into the left atrium and subsequently the left ventricle.

Often, ULTRASOUND during PREGNANCY reveals these significant heart deformities, allowing the neonatal team to be prepared for them at the infant's birth. In many situations initial treatment includes administering PROSTAGLANDINS to maintain a patent ductus arteriosus, which allows some oxygenated blood into the body's circulation.

Congenital heart disease in adults Some forms of congenital heart disease first manifest in adulthood, such as hypertrophic cardiomyopathy and LQTS. Other forms of heart disease in adults may have congenital origins, such as the ARRHYTHMIA disorder WOLFF-PARKINSON-WHITE SYNDROME and some VALVULAR HEART DISEASE. Cardiologists believe that most situations of SUDDEN CARDIAC DEATH reflect undetected congenital heart anomalies, either structural or functional (arrhythmias). With congenital heart disease, whether undetected or previously treated, comes increased risk for ENDOCARDITIS (especially with valve malformations), arrhythmias, and clot formation leading to HEART ATTACK, STROKE, or PULMONARY EMBOLISM.

A growing number of adults had corrective surgery for congenital heart disease as infants or children. Cardiologists do not yet know the long-term effects of these operations or what precautions are necessary to protect cardiovascular health later in life. The generation born in the 1970s was the first to have these options available. As this generation comes into middle age, cardiologists will learn much about how repaired hearts accommodate the routine cardiovascular stresses of life and whether they are more susceptible to acquired forms of heart disease such as CORONARY ARTERY DISEASE (CAD) and HEART FAILURE. At present, the longest survival of infant heart transplantation is 15 years and of adolescent heart transplantation is 16 years. Rejection of the donor heart remains a significant concern, and most cardiologists expect retransplantation will become necessary for most people who receive heart transplants in infancy or childhood.

Symptoms and Diagnostic Path

The most common symptoms of congenital heart disease, notably malformations of the heart, in newborns is cyanosis and difficulty BREATHING. Congenital heart disease not immediately apparent at birth may manifest later in childhood with symptoms such as fainting with physical exertion, shortness of breath with mild activity, slowed growth, rapid heartbeat and respirations, and frequent upper respiratory infections. Young children experiencing shortness of breath often squat, which makes it easier for them to breathe.

Congenital heart disease that manifests in adulthood, such as ASD and hypertrophic cardiomyopathy, often produces symptoms such as PALPITATIONS, shortness of breath, and pulmonary or generalized EDEMA if the heart's pumping capability becomes ineffective (heart failure). The diagnostic path may include ELECTROCARDIOGRAM (ECG), ECHOCARDIOGRAM, and COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI), and CARDIAC CATHETERIZATION.

Treatment Options and Outlook

Minor congenital heart defects may require only watchful waiting. Most ASDs close within 2 years of birth and VSDs by age 7. Septal defects that persist and cause symptoms may require surgery, often via cardiac catheterization to patch the defect. Surgery is the most viable treatment option for most serious malformations of the heart. Surgery may be corrective, in which the OPERATION returns the heart to normal structure and function, or palliative, in which the operation relieves symptoms though does not restore normal structure and function. Surgery may be isolated, in which a single operation corrects the defect, or staged, in which the surgeon performs several sequential operations over a period of time. Some congenital heart malformations require surgery within days of birth, and others within months to 2 or 3 years.

When doctors detect significant congenital defects before or shortly after birth, they often administer prostaglandins to maintain a patent ductus arteriosus. Though in ordinary circumstances a PDA would be a heart defect, in the presence of congenital heart defects PDA allows continued though limited circulation of oxygenated blood to buy time until the infant is stable enough for surgery. In some circumstances the neonatal cardiologist may perform a balloon septostomy to surgically create an ASD, which further allows a mixture of oxygenated and deoxygenated blood to flow from the heart to the body.

Risk Factors and Preventive Measures

Genetic factors are emerging as the likely causes, or at least precipitating circumstances, for many forms of congenital heart disease. There are clear genetic links for conditions such as hypertrophic cardiomyopathy and LQTS, for example, as well as known correlations between specific heart malformations and genetic disorders such as Down syndrome and TURNER'S SYNDROME. As well, the VACTERL constellation of birth defects speaks to genetic underpinnings. Prevention for these kinds of heart problems remains uncertain, though future treatment is likely to include GENE THERAPY.

Some congenital heart malformations occur as the result of maternal infections such as RUBELLA (German MEASLES). Heart defects in infants are more likely to occur with mothers who have DIABETES. Numerous medications, both prescription and over-the-counter, as well as ALCOHOL consumption also cause specific kinds of birth defects. Women who are pregnant or planning to become pregnant should discuss with their doctors any routine medications they take. Many ANTISEIZURE MEDICATIONS and ANTIPSYCHOTIC MEDICATIONS are especially damaging to the developing fetus.

Despite advances in gene technology and knowledge of the body, much congenital heart disease is idiopathic—that is, doctors do not know why it occurs. Studies suggest that folic acid supplementation, which doctors already recommend to reduce the risk for NEURAL TUBE DEFECTS, also reduces the risk for malformations of the heart. Like the neurologic system, the cardiovascular system evolves early in fetal development so most malformations occur in the first weeks of pregnancy. Doctors can detect many heart abnormalities before birth, allowing parents and doctors to make appropriate treatment decisions.

See also CARDIOVASCULAR DISEASE PREVENTION; INFECTION; KAWASAKI DISEASE; SURGERY BENEFIT AND RISK ASSESSMENT; VEIN.

coronary arteries The network of arteries that encircles the HEART to provide its BLOOD supply. The two primary coronary arteries, the right coronary ARTERY and the left coronary artery, branch from the AORTA as it arises from the left ventricle. The left coronary artery is significantly larger and supplies the left heart. It drops along the left atrium, branching at the base of the left ventricle into the left anterior descending (LAD) and circumflex arteries. The circumflex artery wraps behind the heart, further branching into smaller

arteries that trail across the left ventricle. The right coronary artery traverses the right atrium, nourishing the upper right heart. Numerous smaller arteries branch from it, the largest of which is the right marginal artery. The arterial network intertwines across the front of the heart in a network called Vieussens's ring, which is similar in structure and purpose to the CIRCLE OF WILLIS at the base of the BRAIN. The precise pattern of the coronary arteries is unique for each person, however.

The coronary arteries deliver the largest volume of blood to the heart during diastole, the trough phase of the CARDIAC CYCLE during which the ventricles fill with blood, pulling blood from the aortic root as systole draws to a close. About 60 percent of the ventricular ejection goes to the coronary arteries. During systole, the peak of the cardiac cycle during which the ventricles pump blood out, the dynamic forces of the heart's contraction cause the coronary arteries to constrict.

The extensive branching of the coronary arteries provides a fairly substantial level of redundancy for supplying the heart with blood. Even if damage or occlusion blocks one branch or several branches, other arterial branches can deliver blood to the same or nearby areas to cover the deficit. As well, the heart tends to develop collateral circulation in response to arterial damage, a self-repair feature in which new small arteries sprout to extend around the area of damage. These mechanisms can sustain adequate myocardial perfusion (distribution of blood throughout the heart MUSCLE) for a considerable time, even in the face of significant damage to the heart's circulatory structures. As occlusion of the coronary arteries progresses, the collateral circulation of Vieussens's ring extends.

The efficiency of coronary circulation is such that symptoms of oxygen deficiency (notably ANGINA PECTORIS and shortness of breath with exertion) do not become apparent until damage to the coronary arteries drops blood flow to about 30 percent of normal. At this point a cardiologist may recommend ANGIOPLASTY with STENT placement. The standard diagnostic point for the more invasive CORONARY ARTERY BYPASS GRAFT (CABG) is 90 percent or greater occlusion. The symptoms of restricted blood flow become most apparent when occlusion affects the larger branches of the coronary arteries, notably the LAD and circumflex. The primary conditions that affect the coronary arteries are ATHEROSCLEROSIS, called CORONARY ARTERY DISEASE (CAD) when it involves the coronary arteries, and coronary artery spasm, which often results from CAD though may have other causes.

For further discussion of the coronary arteries within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also COCAINE; HEART ATTACK; LIFESTYLE AND CARDIOVASCULAR HEALTH.

coronary artery bypass graft (CABG) A surgical OPERATION to replace diseased CORONARY ARTERIES supplying the HEART with BLOOD. Cardiovascular surgeons began performing CABG to treat severe CORONARY ARTERY DISEASE (CAD), typically following HEART ATTACK, in the 1960s. The operation became feasible with refinements in CARDIOPULMONARY BYPASS technology and surgical technique. In the ensuing decades CABG has become one of the most frequently performed operations in the United States, with surgeons performing more than 300,000 a year. The surgeon may use CABG to replace one to five coronary arteries; three or four is most common (triple or quadruple bypass). The most frequently bypassed coronary arteries are the left anterior descending (LAD), which traverses the front of the heart; the circumflex, which wraps around the heart; and their respective branches.

Weighing the Benefits and Risks

Whether CABG is an appropriate treatment choice depends on numerous variables that include the person's age and general health status, degree and extent of occlusion in the coronary arteries, and the presence of other CARDIOVASCULAR DISEASE (CVD). Variables that strongly influence the procedure's success include lifestyle factors such as cigarette smoking, body fat and weight, physical inactivity, and dietary habits. Other health conditions that affect HEALING, such as DIABETES, are also important considerations, as are conditions affecting the LUNGS such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).

Now that several million Americans have had CABG and researchers have accumulated data

spanning four decades, evidence is emerging that calls into question the ultimate effectiveness of CABG in preventing deaths due to CAD. A number of studies indicate that CABG may not extend LIFE EXPECTANCY or improve QUALITY OF LIFE to the degree cardiologists and others believe it does. Researchers continue to explore all dimensions of this debate.

Surgical Procedure

The typical CABG takes 75 to 90 minutes for the surgeon to perform. The first steps in CABG are to open the chest, initiate cardiopulmonary bypass, and stop the heart. The preferred approach for the grafts is to use the person's own blood vessels to reconstruct the occluded coronary arteries. The most viable vessels for this purpose are the right and left internal mammary arteries, which the surgeon exposes when opening the chest to perform the CABG. These arteries are ideal because they do not require additional incisions to obtain, and there is a good supply of arterial circulation to replace them. As well, the mammary arteries are about the same size as the coronary arteries, allowing them to accommodate the demands the coronary circulation will place on them. The surgeon may be able to craft two and sometimes three grafts using both internal mammary arteries. Because of its size and importance to coronary circulation, the LAD is first in line for an arterial graft. The surgeon needs about 6 inches of graft for each coronary ARTERY bypass created.

When the CABG involves more coronary arteries than the mammary arteries can accommodate, the surgeon typically harvests a segment of the saphenous VEIN from the leg, which requires an incision in the groin. Though effective enough, the saphenous vein graft is less than ideal for service as a coronary artery and is more prone to postoperative complications. Although its size makes it a sturdy vessel, the saphenous vein lacks the muscular construction of an artery and has a greater risk of collapsing or closing than does an arterial graft. As well, some people have residual edema and other complications after surgery in the leg from which the surgeon harvests the vein. An alternative practice is to instead harvest segments of arteries from elsewhere in the body for which there is relatively redundant circulation (other arteries to provide blood supply), such as the radial artery or the brachial artery in the arm. When autografts such as these are not possible, the surgeon may use a synthetic material specially treated to resist clotting. However, synthetic grafts are not as reliable as autografts.

The surgeon sutures (sews) one end of the graft into the AORTA above the occlusion and the other end into the coronary artery below the occlusion to establish the bypassed path of circulation. The surgeon does this for each occluded coronary artery. When the internal mammary artery provides the graft, the surgeon needs only to suture at the distal end because the proximal end is already in place. The diseased coronary artery segments stay in place though will no longer carry blood. When finished bypassing the occluded coronary arteries, the surgeon restores blood circulation through the heart and restarts the heart with a chemical solution or an electrical charge. After making sure the grafts are intact and not leaking, the surgeon closes the chest. Wires hold the ribs and sternum in place, while sutures and staples close the layers of MUSCLE and SKIN.

Risks and Complications

CABG entails numerous risks and complications. Though its frequency gives the perception that it is a routine operation, CABG is a significant major surgery during which the surgeon places the person on cardiopulmonary bypass, cuts through the breastbone and several ribs to expose the heart, stops the heart to reconstruct the coronary arteries, and then restarts the heart and closes the chest. Each step carries its own risks. Collectively, the major risks of CABG include

- air emboli (air bubbles that get into the bloodstream and create blockages), causing heart attack, STROKE, or PULMONARY EMBOLISM
- excessive bleeding during surgery
- bleeding when the surgeon restores circulation through the heart
- inability to restart the heart
- inability to wean from the cardiopulmonary bypass machine when surgery is done
- postbypass neurologic damage with residual consequences that may include cognitive dys-

function, memory impairment, and physical dysfunctions such as localized loss of feeling or function
- rapid restenosis (within six months) of the grafts
- collapse of venous grafts

Improved technology is making other treatment options, notably ANGIOPLASTY, increasingly viable. Some studies suggest that angioplasty with STENT placement, which is significantly less invasive and less expensive than CABG, is equally effective for multiple vessel CAD and in a good number of people lasts as long as CABG. On the other side of the debate, clinical results with all-arterial grafts for CABG show increased reliability. As well, advances in microsurgery and endoscopic surgery are making MINIMALLY INVASIVE CARDIOVASCULAR SURGERY increasingly feasible, allowing surgeons to perform minimally invasive direct coronary artery bypass (MIDCAB) procedures using multiple small incisions rather than fully opening the chest. Some surgeons are using "off-pump" procedures, in which the heart continues to function during the operation, to reduce the risk for neurologic and pulmonary side effects. Others are combining angioplasty with MIDCAB in a procedure called hybrid CABG. Researchers and surgeons continue to study these approaches and methods, comparing outcomes to determine the most appropriate options.

Outlook and Lifestyle Modifications

Most people spend three to five days in the hospital and another four to eight weeks recovering at home before making a full return to regular activities. The improvement in cardiovascular function is apparent immediately for most people. Cardiologists typically recommend cardiac rehabilitation for people who have had CABG, to help establish a structure for any necessary lifestyle modifications. The clinical standard for postoperative care now includes medications such as beta blockers and statins, drugs to stabilize HEART RATE and lower cholesterol blood levels, respectively. Statins also appear to have a stabilizing and strengthening action on the heart, with numerous clinical studies showing that people who take statins following CABG have significantly fewer complications, notably heart attack, after surgery. Cardiologists also urge people to eat nutritiously, get a minimum of 30 minutes of physical exercise each day, stop smoking, and lose weight to achieve a healthy BODY MASS INDEX (BMI). Most people experience complete and uneventful recovery from surgery and return to work and the recreational activities that interest them.

See also CARDIOVASCULAR DISEASE PREVENTION; COGNITIVE FUNCTION AND DYSFUNCTION; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SMOKING CESSATION; SURGERY BENEFIT AND RISK ASSESSMENT.

coronary artery disease (CAD) ATHEROSCLEROSIS of the CORONARY ARTERIES that reduces BLOOD flow to the HEART. About 14 million Americans have CAD, though many of them do not know it until HEART ATTACK strikes. CAD causes 1.2 million heart attacks and more than 600,000 deaths in the United States every year. Autopsy findings show that two thirds of women and nearly half of men who lose their lives to SUDDEN CARDIAC DEATH had unsuspected CAD. Although CAD is more common in people age 60 and older, it is becoming increasingly common among younger people. Genetic factors may underlie CAD in some people, though most often CAD is an acquired condition that is the direct consequence of lifestyle factors such as cigarette smoking, EATING HABITS, and physical inactivity.

HEART ATTACK is a life-threatening emergency. Call 911 immediately with symptoms or when heart attack is possible. Many people delay, wanting to be sure. Waiting can be fatal.

CAD, like generalized atherosclerosis, develops over decades. Many cardiologists believe CAD begins in childhood. The most commonly affected coronary arteries are the left anterior descending (LAD), the circumflex, and their branches. These coronary arteries provide the blood supply for most of the heart MUSCLE, including nearly all of the left ventricle. CAD may affect the right coronary ARTERY as well. Cardiologists classify CAD according to the number of occluded coronary arteries. A coronary artery can be 70 percent occluded before the restricted blood flow impairs

cardiac function, though cardiologists believe reduced OXYGENATION begins with about 50 percent occlusion. The heart's ability to develop collateral circulation, the growth of new arteries, allows CAD to worsen without overtly affecting cardiac function.

CAD develops when ATHEROSCLEROTIC PLAQUE infiltrates the arterial intima, the innermost layer of the arterial wall, and accumulates into deposits called atheromas. The atheromas cause the arterial wall to thicken, reducing its elasticity and thus its ability to contract and expand in response to blood flow needs. Atheromas also protrude into the channel of the artery, reducing the artery's interior diameter (lumen) and reducing the volume of blood the artery can transport. These factors converge to restrict blood flow to the heart, particularly with exertion (such as during physical exercise), and deprive segments of the heart of adequate oxygenation. The result is ischemia, or tissue HYPOXIA. Typically the ischemia eases with rest, as the heart's demand for oxygen diminishes.

Symptoms and Diagnostic Path

The key symptom of CAD is ANGINA PECTORIS, a pressurelike discomfort or pain originating in the central chest and often radiating up the arm into the jaw and through the shoulder area to the back. At this stage, medical or surgical interventions can head off CAD-induced heart attack. For many people, however, the first indication of CAD is heart attack, which can occur when an atherosclerotic coronary artery ruptures or a blood clot lodges in a section of a coronary artery where CAD has narrowed the passageway. The resulting blockage, or occlusion, interrupts blood flow to a portion of the heart and the heart tissue dies.

CARDIAC CATHETERIZATION and ANGIOGRAM provide definitive diagnosis. These procedures allow the cardiologist to visualize the path of blood through the coronary arteries, highlighting constricted or blocked areas. Severe CAD also causes ARRHYTHMIA (disturbance of the heart's electrical activity), which a person may experience as PALPITATIONS and that show up on ELECTROCARDIOGRAM (ECG). Exercise STRESS TEST, particularly radionuclide testing, reveals the functional limitations resulting from the CAD. ECHOCARDIOGRAM often reveals the dysfunction of the walls of the heart served by diseased coronary arteries, as well as decreased heart function if there has already been damage, and with Doppler ULTRASOUND may show restrictions in the flow of blood.

Some cardiologists use MAGNETIC RESONANCE IMAGING (MRI) to visualize the structure and function of the coronary arteries and the rest of the heart. MRI also detects new collateral circulation (angiogenesis). However, anyone who has a PACEMAKER, IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD), stents, ANEURYSM clips, or other internal metallic objects cannot undergo MRI. An advantage of MRI is its ability to represent dimensional cross-sections of the areas of suspected atherosclerotic accumulation. This reveals the extent to which the CAD has caused the arterial wall to thicken.

A variation of CT scan, ELECTRON BEAM COMPUTED TOMOGRAPHY (EBCT) SCAN, can detect calcification in the arterial walls. Calcification indicates long-standing accumulations of plaque that have solidified within the intima, a sign of well-established CAD that, while perhaps not causing symptoms, is significant enough to pose the risk of heart attack. Of equal, and perhaps greater, concern to cardiologists is the accumulation of soft, unstable atherosclerotic plaque, sometimes called vulnerable atheroma. These soft accumulations appear to cause continued irritation to the arterial wall, with resulting clot formation and the risk that the atherosclerotic plaques will rupture, spilling particles and debris into the blood circulation.

Treatment Options and Outlook

Although CORONARY ARTERY BYPASS GRAFT (CABG) remains the leading treatment for CAD in the United States, cardiologists are moving toward less invasive approaches. CABG is an OPEN HEART SURGERY with numerous risks and complications. A number of studies in the late 1990s and early 2000s raised questions as to whether CABG provides a clear benefit over other treatment alternatives such as ANGIOPLASTY, aggressive lipid-lowering therapy, and significant lifestyle modifications. Cardiologists now implement the latter two methods after CABG, and there is increasing evidence that they are equally effective without CABG. Angioplasty, a cardiac catheterization procedure in which a balloon at the tip of a catheter compresses

the occlusion, remains a popular intervention because it is far less invasive than CABG, requires minimal recovery time, and results in immediate improvement of coronary circulation. However, restenosis (return of the atherosclerotic narrowing) is more the norm than the exception and occurs in a fourth to a third of people within six months. Angioplasty with STENT placement (a tiny springlike device that remains at the site of the occlusion to hold pressure against the arterial wall) fares somewhat better. Treatment options and recommendations continue to evolve as new medications and technologies become available.

The most significant long-term consequence of CAD is damage following heart attack, which may or may not improve with CABG. LEFT VENTRICULAR EJECTION FRACTION (LVEF), a calculation of the percent of blood that leaves the heart with each contraction of the left ventricle, projects the extent of disability resulting from heart attack due to CAD. LVEF above 60 percent generally correlates with little loss of cardiovascular function except with extreme physical exertion. Most people with an LVEF greater than 40 percent can return to work and normal activities. LVEF that drops below 40 percent limits the heart's capacity to meet the body's oxygen needs during moderate physical exertion, and below 20 percent restricts nearly all physical activity.

MAJOR RISK FACTORS FOR CAD

age 50 or older	cigarette smoking
DIABETES	family history of young HEART ATTACK
HYPERLIPIDEMIA	HYPERTENSION
OBESITY	PERIPHERAL VASCULAR DISEASE (PVD)
physical inactivity	

Risk Factors and Preventive Measures

The most clear-cut early warning sign for the development of CAD is HYPERLIPIDEMIA (elevated cholesterol and triglycerides blood levels). Hyperlipidemia indicates dysfunction with the body's lipid synthesis and storage mechanisms, which typically results in accumulations of fatty acids along the inner arterial walls. These accumulations irritate and inflame the artery's intima, establishing the foundation for atherosclerotic plaque development. Numerous studies show that lowering blood lipid levels reduces atherosclerotic accumulations, slowing the progression of CAD. DIABETES, HYPERTENSION, and OBESITY accelerate the progression of CAD. The prevalence of CAD in young people alarms health experts, who emphasize that it is never too early to implement a heart-healthy lifestyle.

An important understanding about CAD is that it is a chronic, lifelong cardiovascular condition. Even with CABG or angioplasty, the disease process continues. Treatments aim to slow the progression but so far are not able to prevent it. Lifestyle changes are imperative for people who want to enjoy extended LIFE EXPECTANCY as well as QUALITY OF LIFE. Though the outlook for controlling CAD has never been brighter, CAD remains a major health concern. Lifestyle modifications to improve cardiovascular health, in combination with medical interventions such as ASPIRIN THERAPY and medications to regulate heart function, can significantly impede CAD's progression.

See also CARDIOVASCULAR DISEASE PREVENTION; COENZYME Q10; DIABETES AND CARDIOVASCULAR DISEASE; DIET AND CARDIOVASCULAR HEALTH; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; SMOKING AND CARDIOVASCULAR DISEASE; STROKE.

c-reactive protein A substance the body's tissues release when they become inflamed. Some health experts believe elevated levels of c-reactive protein in the BLOOD may indicate the presence of ATHEROSCLEROSIS. Though cardiologists and researchers have known for some time that inflammatory processes accompany atherosclerosis, studies in the 1990s and early 2000s began to suggest that INFLAMMATION, perhaps due to low-grade INFECTION, might be a contributing cause of atherosclerosis. Elevated blood levels of c-reactive protein in people who have had HEART ATTACKS portend significant increase in risk for subsequent HEART attacks. However, cardiologists are not certain how important elevated c-reactive protein levels are in people who do not appear to have CARDIOVASCULAR DISEASE (CVD). Chronic inflammatory conditions may also elevate c-reactive protein. Cardiologists generally recommend considering a person's level of c-reactive protein in context with other RISK FACTORS FOR CARDIOVASCULAR DISEASE, and base intervention decisions on the overall cardiovascular risk picture.

See also COENZYME Q10; HEART ATTACK; LIFESTYLE AND CARDIOVASCULAR HEALTH; VITAMINS AND HEALTH.

cyanosis A bluish coloration to the lips, nail beds, and SKIN that indicates inadequate oxygenation. Clinically, cyanosis exists when the oxygen saturation of arterial BLOOD drops below 85 percent. Cyanosis may result from conditions that affect the ability of the LUNGS to oxygenate the blood, such as may occur with CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), or that affect cardiac function, such as HEART FAILURE or MYOCARDIAL INFARCTION (HEART ATTACK). Cyanosis may also result from severe ANEMIA and other blood disorders that affect the blood's ability to transport oxygen. Poisoning with mercury or silver can cause the skin to take on a bluish hue, as can certain antipsychotic medications. Doctors call this pseudocyanosis because it is not the result of the blood's oxygen levels.

See also CONGENITAL HEART DISEASE; HEAVY METAL POISONING; HYPOXIA; RAYNAUD'S SYNDROME.

D

DASH eating plan The acronym for "dietary approaches to stop HYPERTENSION." The DASH eating plan is the result of a pair of clinical research studies and features a diet high in fruits, vegetables, low-fat dairy products, whole grain products, and low in fats (particularly saturated fats) and sodium. Numerous studies correlate dietary habits, particularly sodium consumption, with hypertension. The DASH eating plan is appropriate for anyone to follow to maintain cardiovascular health. The plan, available through health-care providers and online from the National Heart, Lung, and Blood Institute (NHLBI) at www.nhlbi.nih.gov, features menus and extensive food choices to help people plan nutritious meals that help lower BLOOD PRESSURE. It also provides guidelines for transitioning to more heart-healthy eating and other lifestyle habits.

See also CARDIOVASCULAR DISEASE PREVENTION; DIET AND CARDIOVASCULAR HEALTH; EATING HABITS; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH.

defibrillation A therapeutic method for delivering an electrical shock to the HEART to restore it to a functional rhythm. Defibrillation is an emergency treatment necessary to prevent death resulting from VENTRICULAR FIBRILLATION (rapid, discordant, and ineffective contractions that fail to pump BLOOD out of the heart). The body cannot survive in ventricular fibrillation for longer than a few minutes, making rapid response essential. The most common causes of ventricular fibrillation are MYOCARDIAL INFARCTION, arrhythmic cardiac disease such as LONG QT SYNDROME (LQTS), ELECTROCUTION, and drowning.

In hospital-based defibrillation, a health-care professional (usually a doctor) places paddles or electrodes on the outside of the chest. The defibrillator machine delivers the determined electrical impulse, generally producing a pronounced jolt in the person's body. The desired effect is for all electrical activity in the heart to momentarily cease, then for the heart to resume normal electrical activity to the extent possible in the context of damage that may have occurred to the heart. The doctor may choose to administer multiple charges, depending on the response and the likelihood for successful restoration of a regular HEART RATE.

In the 1990s a basic portable device, the AUTOMATED EXTERNAL DEFIBRILLATOR (AED) became available. AEDs allow virtually anyone to administer a potentially lifesaving electrical shock to someone who is experiencing ventricular fibrillation. The computerized programming of an AED reads the ELECTROCARDIOGRAM (ECG) of the person to confirm the ventricular fibrillation, then delivers a preset electrical shock. AEDs have saved countless lives.

The risks of defibrillation include electrical BURNS to the person being resuscitated and electrical shock or burns to the person administering defibrillation. Burns may occur at the contact points of the paddles or electrodes and also elsewhere on the body where there are items of metal such as jewelry or, in a hospital setting, monitoring electrodes. As well, anyone in contact with the person or with the bed the person is lying on is at risk for contact electrical shock. The success of defibrillation depends on the cause of the ventricular fibrillation, how long the heart has been in ventricular fibrillation, and the person's overall cardiovascular and general health status.

See also ARRHYTHMIA; CARDIOPULMONARY RESUSCITATION (CPR); CARDIOVERSION.

deep vein thrombosis (DVT) The formation of BLOOD clots in the veins, usually the deep or inte-

rior veins in the legs and lower pelvis. Physical inactivity is the primary cause of DVT. The veins, which are not as muscular as the arteries, rely on the skeletal MUSCLES to support them. The contraction and relaxation of skeletal muscles, such as occurs during walking and other physical activities, helps move blood through the veins. This support and massaging action is particularly important for function of the large veins in the legs, which transport significant volumes of blood toward the HEART against pressure that can reach three times the force of gravity.

During periods of extended inactivity the skeletal muscles relax the tension they otherwise would exert against the veins, allowing the flow of blood to become sluggish. When other problems with the veins exist, such as VENOUS INSUFFICIENCY (inadequate function of the valves in the veins) and VARICOSE VEINS, blood may pool. The pooling provides opportunity for the blood to begin clotting, which can cause the localized occlusion and PAIN that characterizes DVT as well as HEART ATTACK, STROKE or PULMONARY EMBOLISM (blood clot in the LUNG) if a particle of the clot breaks away and travels through the bloodstream.

Birth control pills, even low-DOSE formulations, increase the risk for deep vein thrombosis, most significantly in women who also smoke.

The most effective approach for DVT is prevention, which for many people can be as simple as walking for a few minutes every couple hours during the day, even if only around a desk or lifting the legs as if marching in place. Additional risk factors include OBESITY, DIABETES, VARICOSE VEINS, PERIPHERAL VASCULAR DISEASE (PVD), and cigarette smoking. Doctors may recommend ANTICOAGULATION THERAPY as a further preventive measure to reduce the blood's clotting ability for people who are at risk for developing DVT. Though extended airline flights present a well-popularized risk for DVT, less than one tenth of 1 percent of the 2 million Americans who develop DVT do so as a result of flying.

Once the thrombosis, or clot, develops it blocks the flow of blood, which results in a backup of fluid that seeps into the surrounding tissues (edema). The clot also irritates the walls of the VEIN, causing INFLAMMATION. Symptoms of DVT include

- redness and swelling (edema) at the site of the clot
- tenderness or PAIN at the site of the clot
- FEVER and generalized discomfort

The diagnostic path may include ULTRASOUND or VENOGRAM of the suspected occlusion, which typically provides the visualization necessary to confirm the diagnosis. Treatment typically consists of

- anticoagulation therapy to prevent the clot from enlarging or other clots from forming
- bed rest, with heat to the area to improve circulation, until the clot dissolves
- support stockings

People who have one experience with DVT face increased risk for subsequent DVTs and usually take prophylactic anticoagulation therapy to lower the risk. Lifestyle measures such as daily walking and other physical activity, SMOKING CESSATION, and weight loss if necessary are also key to preventing subsequent DVTs.

See also CARDIOVASCULAR DISEASE PREVENTION; COAGULATION; LIFESTYLE AND CARDIOVASCULAR HEALTH; WALKING FOR FITNESS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

diabetes and cardiovascular disease A leading consequence of DIABETES (type 1 or type 2) is CARDIOVASCULAR DISEASE (CVD), and diabetes is a leading cause of cardiovascular disease. The extent to which diabetes and cardiovascular disease intertwine has caused some health experts to view diabetes as a form of cardiovascular disease. Among people with diagnosed diabetes, more than 95 percent have some form of cardiovascular disease, the most common being HYPERLIPIDEMIA (elevated BLOOD levels of cholesterol and triglycerides) and HYPERTENSION (high BLOOD PRESSURE).

Diabetes causes numerous changes in the body that influence or accelerate the development of cardiovascular disease. Key among them are

- dysfunctions of lipid METABOLISM that result in elevated blood levels of low-density lipoprotein

cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C), and lowered blood levels of high-density lipoprotein cholesterol (HDL-C)

- altered myocardial cell structure and activity, resulting in CARDIOMYOPATHY (myocardial dysfunction)
- increased levels of fibrinogen and clotting substances that increase the blood's tendency to clot, raising the risk for STROKE and HEART ATTACK
- elevated blood GLUCOSE levels damage peripheral blood vessels and the nerves that supply them, raising the risk for PERIPHERAL VASCULAR DISEASE (PVD)
- damage to the glomerular structures of the KIDNEYS, resulting in NEPHROPATHY of diabetes and its slate of complications, key among them being hypertension

Cigarette smoking, itself a significant risk factor for cardiovascular disease, doubles the cardiovascular risk of diabetes in people who smoke and have diabetes. Increasing age is a risk factor for both diabetes and cardiovascular disease. As well, diabetes slows HEALING, increasing the risk for complications with surgical treatment options for forms of cardiovascular disease such as CORONARY ARTERY DISEASE (CAD).

Early diagnosis of INSULIN RESISTANCE with lifestyle and medication, if appropriate, to delay its progression to type 2 diabetes, improves the cardiovascular risk. Once diabetes develops, meticulous control of blood glucose levels slows many of the changes that create increased risk for cardiovascular disease. Aggressive medical interventions such as lipid-lowering medications, ASPIRIN THERAPY, and antihypertensive measures (lifestyle, medication, or both) help moderate risks related to changes in lipid, clotting, and blood pressure mechanisms.

Health experts recommend these targets for people who have diabetes to lower their risk for cardiovascular disease:

- A1c (also called HbA1c or glycohemoglobin)—6 percent or lower (indicates blood glucose levels over time)
- blood pressure—129/79 millimeters of mercury (mm Hg) or lower
- LDL-C —100 milligrams per deciliter (mg/dL) or lower
- BODY MASS INDEX (BMI)—24.9 or lower (healthy weight)
- no smoking
- 30 minutes of moderate physical exercise (such as walking) daily

With diligent control of diabetes and efforts to reduce cardiovascular disease risks, most people who have diabetes can achieve near-normal cardiovascular health for years to decades.

See also CARDIOVASCULAR DISEASE PREVENTION; CHOLESTEROL BLOOD LEVELS.

diet and cardiovascular health The influence of eating habits and food consumption on the health and function of the cardiovascular system. Researchers first conclusively connected diet with cardiovascular health in the 1950s when they recognized that dietary fat was a key source of cholesterol for the body. Health experts issued the first statements about this correlation in the early 1960s. Though researchers now understand much more about how the body acquires and uses NUTRIENTS, they continue to investigate the ways in which dietary factors, independent of as well as in conjunction with other lifestyle variables such as physical exercise, affect cardiovascular health. Much of this research has focused on the role of dietary cholesterol and fats, as excesses of these nutrients in the body are key RISK FACTORS FOR CARDIOVASCULAR DISEASE (notably ATHEROSCLEROSIS).

Through the years doctors have recommended various "diets" (proportions and restrictions of nutrients) to support cardiovascular health and reduce the risk for CARDIOVASCULAR DISEASE (CVD). Research has shown, however, that variety and moderation are factors most important for meeting the body's nutritional needs. The body needs carbohydrates, proteins, and fats—the core nutrients—in varying proportions according to age, activity level, and other variables. Rather than focusing on these proportions, however, health experts recommend instead shifting emphasis to the kinds of foods consumed to

- eat more vegetables, fruits, whole grain products, low-fat dairy products, lean meats (especially fish and poultry)
- eat fewer processed foods, which tend to be high in fats, carbohydrates, and sodium
- balance the number of calories consumed with the number of calories expended through physical exercise

Many people consume far more fats and carbohydrates than they realize, so returning to nutritionally balanced EATING HABITS may at first seem restrictive in the context of a "diet." Portion size is a significant factor as well. The intent of HEART-healthy eating is to supply the body with the nutrients it needs through food choices that appeal to the individual.

The body also needs a wide range of vitamins and minerals to carry out its functions and processes. Minerals such as calcium, potassium, sodium, and magnesium are additionally important for cardiovascular function. These minerals, called electrolytes because they conduct electrical current, facilitate and regulate the electrical activity in the HEART that causes it to contract. The KIDNEYS also use electrolytes to adjust the body's fluid balance, a key aspect of BLOOD PRESSURE regulation. Excessive electrolyte consumption (such as sodium, the primary ingredient of table salt) or insufficient electrolyte consumption (such as results with prolonged VOMITING and DIARRHEA) alters the body's fluid balances, which affects blood pressure and cardiac workload.

In recent years much attention has focused on nutrients that appear to inhibit or even prevent disease processes. Key among them in regard to cardiovascular health are ANTIOXIDANTS, omega fatty acids, and SOY. Antioxidants are chemicals that counter the effects of oxidation, a normal dimension of METABOLISM, in the body. Oxidation represents "spent" fuel, the remnants of energy generation. Oxidation produces molecular fragments called free radicals that randomly attach themselves to other molecules. When they do so, they create molecular structures that are not useful to the body. Researchers believe the accumulation of free radicals is a dominant factor in health conditions such as atherosclerosis and CORONARY ARTERY DISEASE (CAD). Antioxidants bind with free radicals, creating molecular structures the body can eliminate as cellular waste. Vitamins A, C, and E contain antioxidants that may slow the progress of atherosclerosis. Another ANTIOXIDANT, COENZYME Q10, also appears to have a measurable effect in slowing atherosclerotic processes.

Omega fatty acids are polyunsaturated fats—the "good" fats—that help to lower low-density lipoprotein cholesterol (LDL-C) and also help to prevent ATHEROSCLEROTIC PLAQUE from accumulating. Sources of omega fatty acids are cold-water fish such as tuna, salmon, mackerel, lake trout, herring, and sardines. Soybeans and soy-based foods such as tofu contain alpha linolenic acid (ALA), which is an omega fatty acid precursor (the body can convert it to omega fatty acid).

See also CALORIE; CARDIOVASCULAR DISEASE PREVENTION; MINERALS AND HEALTH; NUTRITIONAL ASSESSMENT; OMEGA FATTY ACIDS AND CARDIOVASCULAR HEALTH; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; SOY AND CARDIOVASCULAR HEALTH; VITAMINS AND HEALTH.

echocardiogram A noninvasive, diagnostic ULTRASOUND examination of the HEART that can show the heart's structure and, when combined with Doppler technology, the flow of BLOOD through the heart's chambers and the CORONARY ARTERIES. Echocardiogram is most effective for evaluating VALVULAR HEART DISEASE and structural malformations of the heart such as major congenital deformities, septal defects, and patent ductus arteriosus (PDA).

There is no preparation for a echocardiogram, which uses soundwaves to create visual images. For a transthoracic echocardiogram (TTE), the ultrasonographer places a small amount of gel on the SKIN of the chest to improve contact with the transducer, the device that sends and receives the sound signals. The ultrasonographer then moves the transducer over the surface of the skin. For a transesophageal echocardiogram (TEE), the ultrasonographer numbs the back of the THROAT and passes a narrow cable with a transducer at the tip down the throat into the ESOPHAGUS. A TEE places the transducer as close as possible to the heart, usually to obtain specific images such as to detect septal defects or certain valve malformations.

A computer converts the sound signals into two- or three-dimensional images. Typically the cardiologist does an ELECTROCARDIOGRAM (ECG) at the same time, to correlate the visual images from the echocardiogram with the heart's electrical activity. Sometimes the cardiologist will combine the echocardiogram with an injection of dye, administered intravenously, to better highlight the inner structures of the heart. Echocardiogram or TTE takes 10 to 20 minutes and there is no recovery time necessary after the procedure. People undergoing TEE generally receive sedation before the procedure begins so go to a recovery area after the TEE until fully awake from the sedative and the cardiologist is satisfied there will be no adverse effects.

CONDITIONS ECHOCARDIOGRAM CAN HELP DIAGNOSE OR MONITOR

AMYLOIDOSIS	aortic ANEURYSM
AORTIC STENOSIS	CARDIAC TAMPONADE
CARDIOMYOPATHY	congenital heart malformations
ENDOCARDITIS	HEART FAILURE
HEMACHROMATOSIS	mitral valve prolapse
MYOCARDIAL INFARCTION	MYOCARDITIS
MYXOMA	patent ductus arteriosus
PERICARDITIS	PRIMARY PULMONARY HYPERTENSION
septal defect	VALVULAR HEART DISEASE

See also ANGIOGRAM; COMPUTED TOMOGRAPHY (CT) SCAN; CONGENITAL HEART DISEASE; MAGNETIC RESONANCE IMAGING (MRI).

ectopic beat An extra or additional heartbeat. Ectopic beats can be atrial, called premature atrial contractions (PACs), or ventricular, called premature ventricular contractions (PVCs). PACs are nearly always benign (do not require treatment). Though most PVCs are also benign, persistent PVCs can cause symptoms that do require treatment. CAFFEINE is a common cause of ectopic beats. ALCOHOL use, cigarette smoking, and illicit drugs also can cause or exacerbate ectopic beats.

The most common symptom of ectopic beat is PALPITATIONS, the perception of the heart jumping or skipping a beat though it actually does neither. Ectopic beats are premature—that is, they are normal contractions that occur before their normal rhythm in the CARDIAC CYCLE. The beat that follows, also a normal beat, then feels intensified. An ELECTROCARDIOGRAM (ECG) shows the heart's electri-

cal pattern, including ectopic beats. Their place in the cardiac cycle and their frequency determine whether ectopic beats are part of an ARRHYTHMIA that is potentially harmful. When this is the case, the cardiologist will conduct further diagnostic testing to determine the underlying causes and guide treatment decisions.

Though ectopic beats are really not preventable, reducing factors that contribute to irregularities in the heartbeat, such as caffeine consumption, often help significantly reduce their occurrence.

See also ATRIAL FIBRILLATION; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; PREMATURE VENTRICULAR CONTRACTION (PVC).

electrocardiogram (ECG) A noninvasive diagnostic procedure that converts the heart's electrical activity into patterns of signals typically recorded on paper or displayed on a screen. The ECG is the cornerstone of cardiovascular diagnosis. The normal HEART generates a consistent electrical pattern; nearly anything that goes wrong with the heart shows up on an ECG. A normal heart rhythm produces five predictable fluctuations, called waves, that doctors identify by the letters P, Q, R, S, and T. The main thrust of cardiac activity, ventricular contraction, is the QRS complex.

ECG TRACING

P wave	sinoatrial (SA) node's pacing impulse initiates the CARDIAC CYCLE
Q wave	pacing impulse arrives at the ventricular apex
R wave	main ventricular contraction
S wave	completion of ventricular contraction
T wave	heart's return to readiness for the next cardiac cycle

Reasons for Doing This Test

ECG is a common procedure to assess the function of the heart. It can be baseline, diagnostic, or monitoring. A baseline ECG is generally part of a ROUTINE MEDICAL EXAMINATION and establishes a record of the heart's activity when the heart is presumably healthy. A baseline ECG provides a standard for comparison should there be cardiovascular symptoms the cardiologist needs to evaluate. The cardiologist does a diagnostic ECG to examine the heart's electrical activity as it may correlate to symptoms the person is experiencing. The most common symptoms for which doctors conduct diagnostic ECGs are CHEST PAIN and PALPITATIONS. A monitoring ECG checks the heart's rhythm as a means of evaluating whether medications are working effectively to treat ARRHYTHMIA or to determine whether the heart's function is stable following heart surgery or a cardiac crisis such as HEART ATTACK.

Preparation, Procedure, and Recovery

It is a good idea to avoid CAFFEINE and cigarettes for an hour or so before a scheduled ECG. Doctors generally prefer for ECG to show the heart at rest and prefer people not engage in strenuous exercise within four hours of ECG. Otherwise, ECG requires no preparation and may take place in the doctor's office, at a cardiovascular testing facility, or a hospital. The person lies quietly on a gurney or procedure bed and the ECG technician places about a dozen electrodes on the chest, back, arms, and legs. Talking or moving during the ECG can produce electrical "static" from the muscles. A typical ECG takes about five minutes to complete. Though the reading is immediately available, a cardiologist must interpret it and usually it takes a day for the doctor to report the results back for a routine ECG. The person may go home after the ECG recording is finished.

Variations on the standard ECG procedure include

- Holter monitor or ambulatory ECG, which uses a small, battery-operated unit the person wears on a shoulder strap or belt to monitor the heart's electrical activity over a period of time, typically 24 hours (an ECG technician places the electrodes on the person's chest and back and connects them to the unit)
- Exercise ECG, in which the person walks at varying paces on a treadmill or rides a stationary bicycle while the ECG records the heart's changes in rhythm
- Event ECG, in which the person wears electrodes attached to a small, battery-operated unit that the person turns on during a cardiac event such as palpitations

Risks and Complications

There are no risks or complications associated with ECG. Sometimes the ECG technician must shave a small area of SKIN to allow good electrode contact. Some people who are highly sensitive to adhesive may have a slight skin reaction to the adhesive pad that holds the electrode in place. And some people quickly chill when lying on the procedure table; the ECG technician can cover the person with a warm blanket for improved comfort and to prevent shivering, which can distort the ECG reading. ECG only detects and records the electrical activity of the heart; it does not send any electrical impulses to the heart.

See also AUTOMATED EXTERNAL DEFIBRILLATOR (AED); CARDIOVERSION; DEFIBRILLATION; ECHOCARDIOGRAM.

electrophysiology study (EPS) A diagnostic procedure in which the cardiologist inserts electrodes into the HEART to measure the heart's rhythm and response to various stimuli. The EPS is similar to CARDIAC CATHETERIZATION and provides information to help diagnose disorders of ARRHYTHMIA. The EPS takes place in a hospital or cardiac catheterization laboratory setting and is a same-day procedure for most people. Preparation consists of no food or drink the night before the procedure. The person undergoing the EPS needs a family member or friend to drive to and from the hospital.

After administering a general sedative and a local anesthetic, the cardiologist threads several catheters through an incision in the groin into the femoral vein and then through the arterial network to the heart, watching their progress via FLUOROSCOPY. Once in the heart, the leads on the tips of the catheters send back electrical impulses similar to an ELECTROCARDIOGRAM (ECG). The cardiologist may administer medications or mild electrical impulses to assess the heart's response and ability to return to a normal rhythm.

An EPS takes three to four hours to complete. After the procedure is over, the person goes to a recovery area until he or she is fully awake from the sedative and the cardiologist is satisfied there will be no adverse effects. Sometimes the cardiologist will want the person to stay overnight in the hospital for cardiovascular monitoring. Most people experience mild to moderate discomfort in the groin area where the cardiologist inserted the catheters, and occasionally this is the site for post-procedure bleeding. The EPS provides comprehensive information about the heart's electrical activity.

See also ECHOCARDIOGRAM; STRESS TEST.

endarterectomy An OPERATION to surgically remove accumulations of ATHEROSCLEROTIC PLAQUE (atheromas) from the arteries. The most common site for endarterectomy is the carotid arteries, which carry BLOOD to the head and BRAIN. Endarterectomy is a major surgery done under general ANESTHESIA, typically with 24 to 48 hours of inpatient hospitalization following the OPERATION. During endarterectomy, the surgeon makes a small incision through the SKIN and into the ARTERY at the site of the atheroma, briefly stops the flow of blood through the artery and removes the atheroma, restores blood flow, and sutures the artery closed. Depending on the location and size of the atheroma the surgeon may place a shunt in the artery to allow blood to flow around the site of the atheroma during the operation. The shunt maintains blood supply to the brain and helps prevent atherosclerotic fragments from escaping into the blood flow to the brain.

Endarterectomy is a fairly high risk procedure because of the potential for dislodging fragments of the atheroma during the procedure. When this happens, there is no way to prevent the fragments from traveling up the carotid artery to the brain where they cause STROKE. About 3 percent of people who undergo endarterectomy experience stroke, ranging in severity from imperceptible symptoms to disability or death. Cardiologists recommend endarterectomy when the occlusion is 80 to 99 percent. Studies show that endarterectomy can lower the risk for stroke even when CAROTID STENOSIS does not cause symptoms, though because of the risk that the operation itself can result in stroke, some cardiologists recommend surgery only when the blockage causes symptoms.

See also CORONARY ARTERY BYPASS GRAFT (CABG); POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

endocarditis INFLAMMATION of the ENDOCARDIUM, the lining of the HEART. Viral or bacterial INFECTION

can cause endocarditis; either is potentially life threatening, though bacterial infection is considerably more common. Bacterial endocarditis is a particular risk for people who have certain forms of CARDIOVASCULAR DISEASE (CVD) and may follow bacterial infection in other parts of the body. Pathogenic (infection-causing) BACTERIA may also enter the BLOOD circulation during dental, diagnostic, and surgical procedures that cause bleeding. Endocarditis also occurs as a complication following valve repair or replacement surgery.

CARDIOVASCULAR CONDITIONS THAT INCREASE RISK FOR ENDOCARDITIS

cardiopulmonary shunt	cyanotic CONGENITAL HEART DISEASE
HEART TRANSPLANTATION	hypertrophic CARDIOMYOPATHY
mitral valve prolapse	previous bacterial endocarditis
prosthetic heart valves	RHEUMATIC HEART DISEASE
uncorrected congenital heart malformations	VALVULAR HEART DISEASE

Symptoms may include COUGH, shortness of breath (DYSPNEA), and CHEST PAIN. Mild to moderate FEVER, weight loss, night sweats, and JOINT pain are also common. Symptoms vary with the location and nature of the infection and are often vague, making it challenging for doctors to connect them to the heart. The diagnostic path includes blood cultures to determine the presence of bacteria and ECHOCARDIOGRAM to affirm the inflammation.

Treatment for bacterial endocarditis is intensive antibiotic therapy, administered intravenously in a hospital inpatient setting. Treatment for viral endocarditis is supportive, sometimes requiring hospitalization to administer intravenous fluids and medications to ease the heart's workload until the infection runs its course. Complications of either form include endocardial abscesses, valvular abscesses, and damage to the heart valves. With appropriate treatment most people recover, though some may have residual consequences (such as valve disease) and increased risk for subsequent infections.

See also ABSCESS; ANTIBIOTIC PROPHYLAXIS; MYOCARDITIS; PERICARDITIS; VIRUS.

endocardium The membrane that lines the inner HEART, made up of epithelial cells. The endocardium also covers the heart valves, providing a smooth surface that offers no opportunity for BLOOD cells (particularly platelets) to stick to it as they pass through the heart. The endocardium contains Purkinje fibers, specialized MUSCLE cells that convey the electrical impulses that cause the heart to contract, and collagen fibers, which give the endocardium elasticity. The endocardium is vulnerable to damage from conditions such as RHEUMATIC HEART DISEASE and VALVULAR HEART DISEASE. These conditions can cause irritation that inflames the endocardium, making it susceptible to bacterial INFECTION (ENDOCARDITIS).

For further discussion of the endocardium within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also BACTERIA; MYOCARDIUM; PERICARDIUM; PLATELET.

enhanced external counterpulsation (EECP) A therapy for ANGINA PECTORIS that uses sequential inflation and deflation of cuffs on the legs and pelvis to assist in returning venous BLOOD to the HEART and decreasing cardiovascular resistance in the peripheral arteries. EECP reduces the heart's workload during systole, when the ventricles contract, and increases pressure in the peripheral arterial network during diastole, when the ventricles fill. The net effect is that the body's tissues, including the heart, receive more blood and thus more oxygen with less work from the heart.

Researchers arrived at the concept of EECP in the 1950s. Initial therapeutic efforts were invasive, withdrawing blood from the femoral veins and then returning it. Through the ensuing decades researchers arrived at the method of using compression cuffs around the calves, thighs, and pelvis, alternately inflating and deflating them in a sequence timed with the CARDIAC CYCLE. The cuffs inflate sequentially from the calves to the pelvis during diastole and deflate rapidly and simultaneously during systole. A computer monitors the cardiac cycle via ELECTROCARDIOGRAM (ECG) and coordinates the inflation and deflation of the cuffs accordingly. A therapeutic course involves one hour of EECP daily for 35 hours (typically five days a week for seven weeks), performed at a cardiac clinic or hospital. Most people experience relief from angina for months to 2 or 3 years.

EECP is most appropriate for people who are not receiving adequate relief from medications and would benefit from CORONARY ARTERY BYPASS GRAFT (CABG) but cannot, or choose not, to undergo the surgery. EECP is not appropriate for people who have uncontrolled HYPERTENSION or ARRHYTHMIA or who have bleeding disorders. There are no identified risks associated with EECP. Some people do find the pressure of the counterpulsations somewhat uncomfortable.

See also ANGIOPLASTY; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE.

fibroelastoma A noncancerous, connective tissue tumor that arises from the ENDOCARDIUM, usually on or near a HEART valve. Also called cardiac papillary fibroelastoma, this rare tumor can become serious or life threatening when it interferes with the function of a heart valve. Fibroelastomas most commonly form on or near the aortic valve or the tricuspid valve. They may become large enough to prevent the valve's proper function or to block the flow of BLOOD through the valve. A fibroelastoma may also create turbulence in the heart, allowing blood to pool and clot. Generally fibroelestomas cause no symptoms and cardiologists may detect them incidentally during echocardiogram for other purposes. Because fibroelastomas pose such a significant risk for clotting and STROKE, cardiologists typically recommend surgery to remove them. Cardiologists do not know what causes fibroelastomas, though there is some debate whether they are congenital or acquired.

See also ANTICOAGULATION THERAPY; OPEN HEART SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT; VALVULAR HEART DISEASE.

gallop A pair of extra HEART SOUNDS the cardiologist can hear with the bell of the STETHOSCOPE during diastole, so-named because they occur in rapid succession and sound like the hooves of a galloping horse. The characteristic sound is that of a deep-toned thud. A gallop often exists with tachycardia (rapid, regular HEART RATE) and generally signals ventricular dysfunction such as might follow HEART ATTACK.

See also ARRHYTHMIA.

heart The organ that pumps BLOOD and maintains circulation. About the size of a closed fist, the heart resides in the chest between the LUNGS, slightly offset to the left behind the protective STERNUM (breastbone). It begins beating at about 3 weeks gestational age and during a typical life time contracts about 2.5 billion times. The heart's four chambers contract in coordinated sequence to pump blood to the lungs and to the body, circulating the body's 5- to 6-liter blood supply through the network of arteries and veins of the cardiovascular system up to three times a minute. Synchronized electrical impulses orchestrate the contractions. One-way valves direct the flow of blood into, through, and out of the heart. The right heart handles deoxygenated blood; the left heart handles oxygenated blood.

HEALTH CONDITIONS THAT CAN AFFECT THE HEART

ANEURYSM	AORTIC STENOSIS
ARRHYTHMIA	ATRIAL FIBRILLATION
BUNDLE BRANCH BLOCK	CARDIAC ARREST
cardiac tamponade	CARDIOMYOPATHY
CONGENITAL ANOMALY	CONGENITAL HEART DISEASE
CORONARY ARTERY DISEASE (CAD)	ENDOCARDITIS
FIBROELASTOMA	HEART ATTACK
HEART FAILURE	HYPERTENSION
LONG QT SYNDROME (LQTS)	MYOCARDITIS
MYXOMA	PALPITATIONS
PAROXYSMAL ATRIAL TACHYCARDIA (PAT)	PERICARDITIS
PREMATURE VENTRICULAR CONTRACTION (PVC)	RHEUMATIC HEART DISEASE
SICK SINUS SYNDROME	TORSADE DE POINTES
	VALVULAR HEART DISEASE

The heart's blood supply comes from the CORONARY ARTERIES, which arise from the root of the AORTA and encircle the heart. The heart has a substantial oxygen appetite; the coronary arteries deliver 20 percent of the body's blood supply and 70 percent of the blood's oxygen content to the heart. The heart is a remarkably sturdy and reliable structure that can withstand significant damage and still function adequately to supply the body's needs for oxygen and other nutrients.

For further discussion of the heart within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also LIFESTYLE AND CARDIOVASCULAR HEALTH; RISK FACTORS FOR CARDIOVASCULAR DISEASE.

heart attack The interruption of cardiovascular function. The most common cause of HEART attack is MYOCARDIAL INFARCTION, a blockage of the CORONARY ARTERIES, usually with a BLOOD clot, that disrupts the flow of blood to the heart (MYOCARDIUM). Other causes of heart attack include ARRHYTHMIA, systemic HYPOXIA (such as may occur with drowning or carbon monoxide poisoning), and ELECTROCUTION. About 1.3 million Americans experience heart attacks each year, and 40 percent of them die as a result. Health experts believe significantly more people could survive heart attack with early treatment. Up to 60 percent of people who die from heart attack do so before ever reaching a hospital.

When symptoms suggest heart attack:

- **Call 911**
- **If the person is conscious, have him or her chew an aspirin**
- **If the person is unconscious, has no PULSE or is not BREATHING, begin CARDIOPULMONARY RESUSCITATION (CPR)**
- **Continue CPR until medical help arrives**

When the heart is not beating or cannot beat effectively, oxygen does not get to the body's tissues. Within seconds the body begins to shut down nonessential functions. The BRAIN and the heart itself are the most vulnerable to damage resulting from lack of oxygen; their cells begin to die within three minutes. Immediate CARDIOPULMONARY RESUSCITATION (CPR) can restore OXYGENATION and prevent permanent damage or death. However, the likelihood of survival diminishes by about 10 percent for each minute that passes following the heart's stoppage.

Symptoms and Diagnostic Path

Symptoms vary far more widely than most people realize. The classic symptoms of heart attack are

- intense chest pressure, often crushing
- rapid BREATHING
- profuse sweating (diaphoresis)
- PAIN that radiates from the chest up the left arm
- difficulty breathing or shortness of breath

Many people, and especially women, do not experience classic heart attack symptoms. Instead, their symptoms are more generalized. The danger is that they delay seeking treatment because they are unsure whether they are having a heart attack. Such a delay can be the difference between surviving and dying from a heart attack. Nonclassic heart attack signs include

- NAUSEA and occasionally VOMITING associated with a sense of queasiness
- persistent indigestion (DYSPEPSIA)
- unexplainable anxiety
- vague discomfort in the chest, neck, jaw, or back
- lightheadedness

Warning signs that persist for five minutes require immediate medical assessment. More people survive heart attacks than do not, and more people could survive heart attacks if they received prompt medical treatment. Cardiologists recommend chewing an aspirin tablet at the first signs of possible heart attack, which helps slow the clotting process.

The diagnostic path begins with ELECTROCARDIOGRAM (ECG), which shows the heart's electrical patterns and can usually identify the location of the disrupted function. Regardless of cause, heart attack produces arrhythmias (irregularities of the HEART RATE). Blood tests to measure electrolyte levels and certain proteins that a damaged heart MUSCLE releases also help point to the diagnosis. ECHOCARDIOGRAM can show areas of structural damage to the heart, and CARDIAC CATHETERIZATION with ANGIOGRAM can identify the precise sites of occlusions in the coronary arteries.

Treatment Options and Outlook

Treatment begins with stabilizing the heart's function, which may require various medications including antiarrhythmia medications and drugs that strengthen the heart while reducing the force of its contractions. DEFIBRILLATION may be necessary to restore a functional rhythm to the heart. When doctors can determine within three hours that the cause of the heart attack is a blood clot, they may choose to administer thrombolytic medications ("clot busters") to dissolve the clot as well as anticoagulant medications to prevent further clots. Beyond three hours, thrombolytic medications are not effective. Supportive measures include OXYGEN THERAPY to increase the amount of oxygen in the blood and intravenous fluids to maintain HYDRATION and restore electrolyte balance.

Once the heart recovers, the cardiologist may recommend interventions such as ANGIOPLASTY or CORONARY ARTERY BYPASS GRAFT (CABG) to restore adequate circulation to the heart. Other treatments typically include medications to help regulate the heartbeat and strengthen the heart, and lifestyle modifications for improved cardiovascular health. Treatment also targets any identified underlying causes of the heart attack such as HYPERTENSION (high BLOOD PRESSURE) and ATHEROSCLEROSIS. Current treatment protocols recommend nearly everyone who has a heart attack take statin medications afterward. Statins are lipid-lowering medications that can reduce CHOLESTEROL BLOOD LEVELS, notably low-density lipoprotein cholesterol (LDL-C) by 30 to 40 percent within three months. Statins also help strengthen the heart. Other medications may include beta blockers or calcium channel blockers to lower blood pressure and regulate rhythm.

Depending on the heart attack's severity (the extent of damage to the heart), a person may return to regular activities within a few weeks or require several months to recuperate. Most people benefit from a structured CARDIAC REHABILITATION program.

Risk Factors and Preventive Measures

The primary risk factors for heart attack are CORONARY ARTERY DISEASE (CAD) and hypertension. Many people are unaware that they have either one, so heart attack becomes the first recognition that these conditions exist. Regular ROUTINE MEDICAL EXAMINATION, including tests to measure cholesterol blood levels and blood pressure, help detect these conditions in their early stages, when therapeutic intervention can thwart their progression to life-threatening events such as heart attack and STROKE. Key preventive measures include daily physical exercise, nutritious eating habits, WEIGHT LOSS AND WEIGHT MANAGEMENT, SMOKING CESSATION, and management of conditions such as hypertension and DIABETES.

See also CARDIOVASCULAR DISEASE PREVENTION; LIFESTYLE AND CARDIOVASCULAR HEALTH; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; ROUTINE MEDICAL EXAMINATION.

heart failure The inability of the HEART to adequately pump BLOOD. Heart failure may affect the right heart (pulmonary circulation), left heart (body circulation), or total heart. Heart failure, occasionally called by its antiquated name dropsy, is a consequence of longstanding CARDIOVASCULAR DISEASE (CVD) that has damaged the structure of the heart. About 5 million Americans live with heart failure.

CONDITIONS THAT CAN CAUSE HEART FAILURE

ATHEROSCLEROSIS	CARDIOMYOPATHY
certain arrhythmias	CONGENITAL HEART DISEASE
CORONARY ARTERY DISEASE (CAD)	HEART ATTACK
HYPERTENSION (high BLOOD PRESSURE)	long-term ALCOHOL abuse
PRIMARY PULMONARY HYPERTENSION	VALVULAR HEART DISEASE

Symptoms and Diagnostic Path

The key symptoms of heart failure are shortness of breath (DYSPNEA) and fluid retention (edema). Because symptoms come on gradually as the heart failure progresses, many people are unaware of them until they notice fatigue, weakness with exertion, rapid or unexplained weight gain, and frequent URINATION. Right heart failure tends to produce peripheral edema (swelling of the lower legs, ankles, and feet). Left heart failure tends to produce central edema (fluid accumulation in the LUNGS), also known as congestive heart failure. Progressive heart failure generally affects the total heart, though right or left failure may be dominant. The diagnostic path typically includes chest X-RAY, which shows fluid accumulation in the lungs and enlargement of the heart, as well as ELECTROCARDIOGRAM (ECG) to assess the heart's electrical activity. Heart failure often causes ARRHYTHMIA. ECHOCARDIOGRAM shows the heart's function and size.

Treatment Options and Outlook

Treatment targets any causative cardiovascular conditions, such as CORONARY ARTERY DISEASE (CAD) and HYPERTENSION. Surgery may correct valve dysfunctions or previously undetected congenital abnormalities such as septal defect. Medications can effectively manage heart failure for many years, allowing people to work and enjoy recreational activities. However, as heart failure progresses, it imposes greater restrictions on physical activity. People who have end-stage heart failure may benefit from a ventricular assist device (VAD), a mechanical pump implanted in the chest cavity that aids the heart in pumping blood. This allows the heart to rest and sometimes to recuperate. The VAD also can serve as a bridge to HEART TRANSPLANTATION, another treatment option for end-stage heart failure.

Risk Factors and Preventive Measures

Underlying cardiovascular conditions are the most important risk factors for heart failure, particularly those that are undiagnosed or poorly managed (notably hypertension and CAD). Lifestyle measures to prevent cardiovascular disease, such as daily physical exercise and not smoking, reduce the likelihood of heart failure as well. CARDIAC REHABILITATION following heart attack can restore heart function to the extent possible. Other preventive measures include careful management of

MEDICATIONS TO TREAT HEART FAILURE

Medication Type	Representative Medications	Effects
angiotensin II receptor inhibitors	losartan, valsartan, telmisartan	dilate arteries; lower BLOOD PRESSURE
angiotensin-converting enzyme (ACE) inhibitors	captopril, enalapril, ramipril, benazepril, monopril	dilate arteries; lower blood pressure; slow progression of HEART FAILURE
anticoagulants	warfarin, heparin, aspirin	reduce blood's tendency to clot
beta blockers	carvedilol, metoprolol, propranolol, sotalol, timolol	regulate HEART RATE
calcium channel blockers	amlodipine	dilate arteries; lower blood pressure
diuretics	hydrochlorothiazide, furosemide, bumetanide, metolazone	reduce fluid accumulations (edema)
inotropics	digoxin, digitoxin	strengthen heart MUSCLE; decrease heart's workload
vasodilators	nitroglycerin, isosorbide, hydralazine, minoxidil	relax and open blood vessels

conditions such as DIABETES and OBESITY (including WEIGHT LOSS AND WEIGHT MANAGEMENT) that can lead to cardiovascular disease.

See also CARDIOVASCULAR DISEASE PREVENTION; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; VENTRICULAR ASSIST DEVICES (VADS).

heart murmur The sound of BLOOD flowing through an abnormal opening in the HEART. Heart murmur is a sign rather than a condition. Transient heart murmurs are common and benign, generally signaling an occasional or circumstantial incomplete valve closure, and do not require further evaluation or treatment. Transient heart murmurs may be present during FEVER, especially in children, and in pregnant women. Heart murmur sometimes occurs with noncardiovascular conditions such as ANEMIA and HYPERTHYROIDISM.

Murmurs are likely to herald cardiovascular disorders when they appear with symptoms such as shortness of breath (DYSPNEA) with exertion. Persistent heart murmurs may indicate a heart condition that requires treatment. The most common cardiac causes of murmur are

- VALVULAR HEART DISEASE, in which a valve in the heart fails to close properly and blood flows back through it
- atrial septal defect or ventricular septal defect, in which there is an opening in the septum, or heart wall, between the two atria or the two ventricles that allows blood to flow directly between the affected chambers
- AORTIC STENOSIS or pulmonary ARTERY stenosis, in which narrowing of the artery causes blood to back up

Persistent heart murmurs may also be present in GENETIC DISORDERS such as MARFAN SYNDROME or CHROMOSOMAL DISORDERS such as DOWN SYNDROME (trisomy 21). These conditions often have cardiovascular components. The diagnostic path typically includes ELECTROCARDIOGRAM (ECG) and ECHOCARDIOGRAM or COMPUTED TOMOGRAPHY (CT) SCAN and may include more invasive diagnostic procedures such as CARDIAC CATHETERIZATION. Treatment targets the underlying cause of the murmur and may include medications or an OPERATION to repair the problem.

See also OPEN HEART SURGERY; RHEUMATIC HEART DISEASE.

heart rate The number of times in a minute that the HEART completes a CARDIAC CYCLE, commonly measured as the PULSE. At rest, the healthy adult heart beats between 60 and 80 times per minute. The heart rate of a person who is aerobically fit is slower because the heart is more efficient and can pump more blood with each contraction. CARDIOVASCULAR DISEASE (CVD) that reduces CARDIAC CAPACITY often results in an increased heart rate as the heart attempts to compensate for decrease in volume per beat. An unusually rapid heart rate at rest is tachycardia; an unusually slow heart rate at rest is bradycardia. Noncardiac health conditions also can affect heart rate. Heart rate may increase with HYPERTHYROIDISM and decrease with HYPOTHYROIDISM. Other factors that increase heart rate include physical activity, stress, fear, and FEVER.

An aerobically fit heart can increase its pumping volume at a lower increase in heart rate to meet the body's oxygen needs during physical activity or exercise. The heart's maximum heart rate is the upper limit of cardiac function and declines with increasing age. Health experts recommend physical activity for aerobic conditioning that puts the heart rate between 25 and 75 percent of maximum heart rate for 20 to 30 minutes. An individual's target heart rate varies according to AEROBIC FITNESS level. The most effective method for reaching and staying within the target heart rate during exercise is to use a heart monitor, which counts the heartbeats of the person wearing it.

See also AEROBIC EXERCISE; AEROBIC FITNESS; ARRHYTHMIA; EXERCISE AND HEALTH; FITNESS LEVEL; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; WALKING FOR FITNESS.

heart sounds The sounds of the opening and closing of the heart's valves and the passage of BLOOD through them. HEART sounds are an important component of physical diagnosis for cardiovascular conditions. Doctors listen to them using a STETHOSCOPE.

The classic *lubb dupp* sounds are the normal heart sounds in a healthy adult. These are the first and second heart sounds, designated S1 and S2. S1 represents the closing of the tricuspid and mitral valves between the atria and the ventricles. S2 represents the closing of the pulmonary and aortic valves as blood leaves the right and left ventricles, respectively. Other heart sounds are abnormal in adults, occurring only with certain health (and usually heart) conditions. They include

- S3, sometimes called a pericardial knock, indicates a dilated ventricle and ventricular dysfunction such as may occur with CARDIOMYOPATHY (though S3 may be a normal heart sound in young children) or HEART FAILURE. S3 is a low-pitched, vibrational sound the doctor can hear using the bell of the stethoscope.
- S4, indicates abnormal MUSCLE tissue in the heart such as might occur with MYOCARDIAL INFARCTION or hypertrophic cardiomyopathy. S4 also may occur with ISCHEMIC HEART DISEASE (IHD) and HYPERTENSION. Like S3, S4 is a low-pitched vibration the doctor hears with the bell of the stethoscope.
- A click is a high-pitched tone following S1 that indicates improper closing of a valve such as might occur with AORTIC STENOSIS or pulmonary artery stenosis, particularly when these conditions are congenital.
- A snap is a sharp sound following S2 that is typical with mitral stenosis.
- A murmur is a whooshing or whispering sort of sound that indicates blood flowing back through an incompletely closed valve. The timing and quality of the murmur's sound help determine which valve is dysfunctional. Heart murmurs are common and often have no cardiovascular significance, though persistent murmurs may indicate VALVULAR HEART DISEASE.

The cardiologist may choose to further investigate persistent abnormal heart sounds using ELECTROCARDIOGRAM (ECG), ECHOCARDIOGRAM, and other diagnostic procedures depending on the person's symptoms and cardiovascular history.

See also AUSCULTATION; CONGENITAL HEART DISEASE; HEART MURMUR.

heart transplantation The replacement of a diseased HEART with a healthy heart from a deceased donor. Heart transplantation is a therapeutic

option for severe CONGENITAL HEART DISEASE such as hypoplastic left heart syndrome (HLHS) as well as hypertrophic CARDIOMYOPATHY and end-stage HEART FAILURE. South African heart surgeon Christiaan Barnard (1922—2001) performed the first human heart transplantation in 1967, when he replaced the badly diseased heart of 53-year-old Louis Washkansky with the healthy heart of 25-year-old Denise Darvall who died in an accident. Though Washkansky lived only 18 days with the new heart, the OPERATION catapulted cardiovascular medicine into a new era. Today cardiovascular surgeons perform about 2,200 heart transplant operations a year in the United States. More than 70 percent of donor heart recipients live at least 5 years; the longest survival is 24 years.

DONOR HEART SHORTAGE

More than 4,000 people wait on the donor HEART list, yet donor hearts will be available for little over half of them. Many people who could be heart donors are not. Surgeons must place the donor heart in the recipient within four hours of the donor's death. Because many people have not made decisions in advance about organ donation, the time it takes to obtain the family's permission may make it too late to use the heart. There is no cost to the donor's family for removal of donated organs.

Heart transplant recipient criteria Though many people may become critically ill with CARDIOVASCULAR DISEASE (CVD), heart transplantation is a viable option primarily for end-stage heart failure. Health experts estimate that heart transplants could save the lives of 25,000 or more people each year who currently die as a result of heart failure, though the severe shortage of donor hearts restricts heart transplantation to people who are dying from heart failure yet are otherwise healthy—people who have both great need and great potential for survival. Conditions that may result in heart transplantation include

- end-stage heart failure for which medical therapies are ineffective, typically resulting from inoperable CORONARY ARTERY DISEASE (CAD), inoperable VALVULAR HEART DISEASE, and cardiomyopathy
- life-threatening ARRHYTHMIA that does not respond to other treatment
- inoperable congenital malformations of the heart, such as HLHS and tetralogy of Fallot, when surgical reconstruction of the heart either fails or is not likely to be successful

Though numerous clinical criteria establish the severity of cardiovascular status, typically LEFT VENTRICULAR EJECTION FRACTION (LVEF) that falls below 25 percent is the decisive factor. LVEF represents the percent of blood in a full left ventricle that the heart pumps into the body with each contraction of the left ventricle. The amount of blood that enters the body is the stroke volume. A normal LVEF is 55 percent or higher; an LVEF of 40 percent is moderately debilitating. At 25 percent, there are symptoms of cardiovascular distress (such as shortness of breath and ANGINA PECTORIS) even at rest and the person is unable to perform most physical activities.

As well, there are general eligibility criteria to ensure optimal chance for survival after transplantation. These general criteria for heart transplantation include

- expectation of one year or less survival
- age 65 or younger (though an older person who meets all other criteria may be accepted as a recipient)
- otherwise good health
- capable of and willing to comply with lifelong medical care

Various health circumstances tend to preclude consideration for heart transplantation, though they are not absolute. Called comorbid conditions, these include

- INSULIN-dependent DIABETES with NEPHROPATHY, NEUROPATHY, or RETINOPATHY (damage to KIDNEYS, nerves, or eyes)
- primary irreversible kidney disease (not related to cardiovascular disease)
- primary irreversible LIVER disease such as CIRRHOSIS (not related to cardiovascular disease)
- cancer within the previous five years (except SKIN)

- PERIPHERAL VASCULAR DISEASE (PVD) with symptoms such as INTERMITTENT CLAUDICATION
- TRANSIENT ISCHEMIC ATTACK (TIA)
- PRIMARY PULMONARY HYPERTENSION (PPH), CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), EMPHYSEMA, or severe ASTHMA
- OBESITY

Though none of these criteria is absolute, because of the extreme limited availability of donor hearts cardiologists must be able to justify exceptions. Heart transplantation centers set their own criteria, which may be more or less stringent than the general criteria. Many heart transplantation centers are reluctant to approve individuals who are not likely to maintain the rigorous therapeutic and lifestyle regimens necessary following transplant. In infants and children, heart transplantation is an option for nonsurvivable major congenital anomalies. The shortage of donor hearts severely limits heart transplantation in infants, however.

The donor heart The United Network for Organ Sharing (UNOS) maintains donor lists for all transplant circumstances (except corneas and SKIN) in the United States. UNOS coordinates the acquisition and distribution of donor organs according to strict guidelines and policies that direct available organs to the sickest people on the waiting lists for whom criteria match. Regional transplantation centers carry out the acquisitions and distributions. People waiting for heart transplants must be available 24 hours a day and must be able to reach their transplantation centers within two hours.

The donor's BLOOD TYPE must be the same as the recipient's, and the donor and recipient need to be similar in body size and weight. The heart of a donor who is six feet, four inches tall will not fit in the chest cavity of a recipient who is five feet, three inches tall. Similarly, the heart of a small donor cannot meet the cardiovascular needs of a large recipient. Gender, race, and ethnicity do not matter. The donor's heart must be healthy, and the donor must be under age 65 and free from serious or communicable diseases. Most donor hearts come from people who lose their lives in accidents that cause irreversible, overwhelming BRAIN damage. A specialized surgical team carefully harvests the heart in the operating room, after certifying brain death though while cardiovascular function continues, and places the heart in a cold electrolyte solution to preserve it during transport to the recipient's medical center. The heart remains viable for four to six hours.

Surgical Procedure

The heart transplant operation typically takes three to five hours. The surgeon opens the chest with a large incision lengthwise over the STERNUM and cuts the sternum with a saw to open the chest. After placing the person on CARDIOPULMONARY BYPASS (mechanical oxygenation and circulation of the blood), the surgeon removes the diseased heart. There are several methods for doing this; the most common is to cut away all of the heart except the back walls of the atria to preserve the connections to their blood vessels (the superior VENA CAVA, inferior vena cava, and pulmonary VEIN). Respectively, the surgeons cut away the back of the donor heart to match and suture the donor heart into place beginning with the left atrium. The great arteries—the AORTA and the pulmonary ARTERY—are the final structures the surgeon attaches. The heart spontaneously begins to beat when the surgeon restores blood flow. The surgeon closes the sternum with wire to hold it together while it heals, and closes the outer chest tissues with sutures or staples. Most people remain in the hospital up to 10 days following surgery.

Risks and Complications

Heart transplantation entails numerous risks and complications during (operative) and following (postoperative) the surgery. Operative risks include bleeding, air embolism (air that escapes into the bloodstream from the cardiopulmonary bypass), unexpected anatomic incompatibilities (the donor heart does not "fit"), and inability to restore cardiac function. The most significant complications following heart transplantation, which also account for the greatest number of deaths, are INFECTION and rejection. Arrhythmias and other dysfunctions of the heart sometimes occur, though typically respond to medications. Occasionally the transplanted heart fails to function, a circumstance called graft failure. Immediate retransplantation is generally the only treatment.

People who have transplanted hearts are vulnerable to rapidly progressive CAD, HYPERTENSION, and arrhythmias. The transplanted heart is denervated—though it contains its own conductive NERVE network to convey electrical pacing impulses, it does not have nerves connecting it to the body's sympathetic nerve pathways. Normal NERVOUS SYSTEM mechanisms (the sympathetic nerve pathways) that typically regulate HEART RATE and cardiac workload are not functional in the transplanted heart, though in some people reinnervation occurs over time. The absence of sympathetic nerve pathways also means the person does not experience angina pectoris, a primary symptom of CAD and ISCHEMIC HEART DISEASE (IHD). This increases the risk for silent HEART ATTACK. Cardiologists closely monitor the transplanted heart for any signs of CAD, and also routinely prescribe lipid-lowering medications to help prevent CAD from developing.

Other long-term risks include an increased risk for cancer, most commonly skin and lymphatic, because of the IMMUNOSUPPRESSIVE THERAPY. Infection and rejection remain risks as well. Rejection can be acute (come on suddenly and severely) or chronic (persist in a low-grade fashion over time, or come and go). Many cardiologists believe the accelerated CAD process also results from immunosuppression rather than the conventional factors.

Outlook and Lifestyle Modifications

Most people remain hospitalized for 5 to 10 days after the transplant operation, while the new heart stabilizes and the surgical wounds start to heal. During this time doctors initiate IMMUNOSUPPRESSIVE THERAPY, ANTICOAGULATION THERAPY, and various medications to support the heart's function during early HEALING. All transplant recipients will need to take IMMUNOSUPPRESSIVE MEDICATIONS for the remainder of their lives to prevent their bodies from rejecting the donor organ.

Most heart transplant recipients will continue taking other cardiovascular medications to support cardiovascular efficiency. The transplanted heart's denervation affects its ability to adjust to changing cardiovascular needs in the body, such as with exercise. Many people require a PACEMAKER after transplantation to maintain an adequate heart rate and appropriate heart rhythm. Heart transplantation requires lifetime medical follow-up, usually annual CARDIAC CATHETERIZATION and other diagnostic procedures to assess the heart's function.

Most heart transplant recipients return to their regular work and leisure activities, including sexual activity, gradually over two to three months. The cardiologist may restrict certain kinds of strenuous physical activity depending on the heart's ability to respond to the body's increased oxygen needs. The healing process is generally quite rapid as full cardiovascular function returns the body to its normal function. CARDIAC REHABILITATION helps restore the body to a level of physical STRENGTH and AEROBIC FITNESS that further supports cardiovascular health. Moderate daily physical exercise (such as walking), nutritious eating habits, and total abstinence from smoking are essential.

See also CARDIOVASCULAR DISEASE PREVENTION; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; OPEN HEART SURGERY; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; QUALITY OF LIFE; SEXUAL ACTIVITY AND CARDIOVASCULAR DISEASE; TRANSMYOCARDIAL LASER REVASCULARIZATION (TMLR); VENTRICULAR ASSIST DEVICES (VADS).

heredity and heart disease The genetic variables that influence the development of CARDIOVASCULAR DISEASE (CVD). Some forms of cardiovascular disease are entirely hereditary and develop without influence of lifestyle factors. Among them are hypertrophic CARDIOMYOPATHY, LONG QT SYNDROME (LQTS), WOLFF-PARKINSON-WHITE SYNDROME, and familial HYPERLIPIDEMIA. There appear to be few interventions, medical or lifestyle, that can prevent these conditions. Early diagnosis allows for optimal medical management. Researchers suspect that undiagnosed hereditary conditions, notably ARRHYTHMIA disorders, account for up to 25 percent of SUDDEN CARDIAC DEATH in the United States.

Congenital malformations of the HEART often accompany GENETIC DISORDERS or CHROMOSOMAL DISORDERS. Septal defect is common in children who have DOWN SYNDROME (trisomy 21), for example. Most people who have MARFAN SYNDROME, a hereditary connective tissue disorder, have cardiovascular abnormalities including malformed heart valves and arterial walls that lack connective tissue, weakening them and making them vulnerable to ANEURYSM.

As well, there are correlations, though researchers do not fully understand them, among BIRTH DEFECTS involving the heart that occur in conjunction with specific birth defects affecting other body structures. About a third of infants born with ESOPHAGEAL ATRESIA (incomplete formation of the ESOPHAGUS) also have the heart malformation patent ductus arteriosus (PDA). Heart malformations are also common in children who have NEURAL TUBE DEFECTS such as SPINA BIFIDA. These correlations strongly suggest GENE mutations.

Gender and race are other hereditary factors that influence the development of cardiovascular conditions. Men, until about age 60, have three to five times the risk for CORONARY ARTERY DISEASE (CAD) and HYPERTENSION (high BLOOD PRESSURE). Men under age 60 are also more likely to have HEART ATTACK or STROKE. The risk for cardiovascular disease is exponentially higher among African Americans. Hypertension is the leading cause of stroke and kidney failure among African American men between the ages of 35 and 50.

Other forms of cardiovascular disease that tend to "run in the family" may have genetic underpinnings that manifest with interplay from certain lifestyle factors such as cigarette smoking, lack of physical exercise, and eating habits. Such cardiovascular conditions include hypertension (high blood pressure), ATHEROSCLEROSIS, CAD, and PERIPHERAL VASCULAR DISEASE (PVD). Evidence is very strong that appropriate lifestyle interventions can delay or even prevent the onset of such conditions despite any genetic predisposition.

See also CARDIOVASCULAR DISEASE PREVENTION; LIFESTYLE AND CARDIOVASCULAR HEALTH; RISK FACTORS FOR CARDIOVASCULAR DISEASE.

homocysteine An amino acid in the BLOOD that the body's METABOLISM of the essential amino acid methionine produces. (An essential amino acid is one the body cannot synthesize itself but must obtain from dietary sources.) B vitamins and folic acid are necessary to break down homocysteine. Accumulation of homocysteine in the blood circulation appears to accelerate development of ATHEROSCLEROSIS. In the mid-1990s researchers discovered a connection between elevated blood homocysteine levels and early atherosclerosis. Doctors had known since the 1960s of a rare genetic condition, homocystinuria, that caused extensive atherosclerotic disease in teens and young adults. But new research led them to correlate atherosclerosis with elevated homocysteine levels in adults who had no known genetic foundation for them.

Some researchers believe that elevated homocysteine irritates the inside walls of the arteries. The irritation causes INFLAMMATION, which opens the way for ATHEROSCLEROTIC PLAQUE to infiltrate the intima, the innermost layer of the arterial walls. People between the ages of 45 and 60 who have significant atherosclerosis or CORONARY ARTERY DISEASE (CAD) often have elevated homocysteine levels. In people who have elevated homocysteine levels, atherosclerosis may develop more rapidly and at earlier ages. However, research studies as yet have not established a cause and effect relationship between elevated homocysteine and early atherosclerosis.

A blood test can measure the homocysteine level in the blood. Most doctors view homocysteine as a risk factor for CARDIOVASCULAR DISEASE (CVD), though not one that is alone significant enough to cause cardiovascular disease. They recommend people receive the minimum daily amounts of vitamins B_6, B_{12}, and folic acid through dietary sources when possible and with supplements if necessary, as a matter of general health as well as to aid in breaking down homocysteine. People who have elevated homocysteine levels along with other RISK FACTORS FOR CARDIOVASCULAR DISEASE should do what they can to reduce their overall risks, though health experts do not advise folic acid supplementation beyond the recommended intake (400 micrograms daily for an adult) as a preventive measure for cardiovascular health. Adequate folic acid intake appears essential for numerous health reasons, and may help reduce the risks for other health conditions.

See also COENZYME Q10; DIET AND CARDIOVASCULAR HEALTH; NEURAL TUBE DEFECTS.

hyperlipidemia A disorder of lipid METABOLISM, also called hyperlipoproteinemia, that results in abnormally high levels of cholesterol, triglycerides, and lipoproteins in the BLOOD circulation. Hyperlipidemia is a key contributor to ATHEROSCLEROSIS, CORONARY ARTERY DISEASE (CAD), and PERIPHERAL VAS-

CULAR DISEASE (PVD). Hyperlipidemia also can cause health conditions such as PANCREATITIS. Some forms of hyperlipidemia are familial or hereditary and may manifest regardless of lifestyle. Medications can cause hyperlipidemia as well, notably oral contraceptives (birth control pills), estrogen therapy, thiazide diuretics, and corticosteroids. Hyperlipidemia may also be a sign of other health conditions such as CUSHING'S SYNDROME, DIABETES, LIVER dysfunction, and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). In most people who have hyperlipidemia, however, it appears that lifestyle factors interact with genetics.

Doctors measure lipid levels in the blood and consider them individually as well as in correlation to each other in determining the extent of cardiovascular risk they pose. There are five types, or classifications, of hyperlipidemia that have unique presentations, genetic factors, and characteristic progressions. The five types of hyperlipidemia are

- type I, a rare inherited lipid disorder sometimes called apolipoprotein C-II deficiency, in which very low density lipoprotein (VLDL) triglycerides and lipids called chylomicrons accumulate in the bloodstream
- type II, a common group of familial or acquired lipid disorders, sometimes called hypercholesterolemia, in which low-density lipoprotein (LDL) cholesterol levels in the blood are elevated, and there may be apolipoprotein B deficiency
- type III, an uncommon familial lipid disorder in which VLDL and total cholesterol are elevated, usually resulting from apolipoprotein E deficiency
- type IV, a common familial or acquired lipid disorder in which blood lipid elevations are associated with OBESITY and decline with weight loss
- type V, an uncommon lipid disorder in which triglycerides are extremely elevated, though other blood lipid levels are fairly normal, and that frequently causes pancreatitis

Most forms of hyperlipidemia can occur without evidence of familial or hereditary connections.

Symptoms and Diagnostic Path

Hyperlipidemia itself does not cause symptoms. Doctors detect hyperlipidemia through blood tests, conducted after an 8- to 12-hour fast, that measure blood lipid levels. The pretest fast is important to remove any dietary influences. Elevated blood lipid levels are diagnostic. When blood lipid levels are extremely high and other risks for CARDIOVASCULAR DISEASE (CVD) exist, the doctor may recommend further evaluation to look for CAD, PVD, and other atherosclerotic conditions.

Treatment Options and Outlook

Regardless of the cause of elevated blood lipids, the important therapeutic goal is to reduce them. For people who have mild to moderate elevations and no other cardiovascular disease risk factors (including family history of hyperlipidemia), lifestyle changes alone may be enough to bring lipid levels down to acceptable ranges. Doctors are generally willing to give this approach about two months to lower blood lipid levels. When lipid levels remain elevated despite lifestyle changes, or the person cannot make adequate lifestyle changes, health experts recommend lipid-lowering medications. Lowering blood lipids results in a significant decrease in cardiovascular risk, especially for early CAD and HEART ATTACK (before age 40).

MEDICATIONS TO TREAT HYPERLIPIDEMIA (LIPID-LOWERING MEDICATIONS)

Statins		
atorvastatin (Lipitor)	fluvastatin (Lescol)	lovastatin (Mevacor)
pravastatin (Pravachol)	simvastatin (Zocor)	
Fibrates		
clofibrate (Atromid-S)	fenofibrate (Tricor)	gemfibrozil (Lopid)
Bile acid sequestrants		
cholestyramine (Questran, Prevalite)	colesevelam (WelChol)	colestipol (Colestid)
Selective cholesterol absorption inhibitors		
ezetimibe (Zetia)		

Many doctors recommend niacin, either alone or in combination with lipid-lowering medications, to help lower blood lipid levels. Niacin

decreases the liver's production of VLDL and low-density lipoprotein (LDL), which curtails triglyceride production. Niacin can cause unpleasant facial flushing and tingling sensations in the fingers and toes, however, even at low doses.

Risk Factors and Preventive Measures

The key risk factors for hyperlipidemia are family history and lifestyle habits. Most people can lower their risk for hyperlipidemia through eating habits and exercise. Even in combination with medication, lifestyle factors are important for maintaining healthy lipid metabolism.

See also CARDIOVASCULAR DISEASE PREVENTION; CHOLESTEROL BLOOD LEVELS; CHOLESTEROL, ENDOGENOUS; C-REACTIVE PROTEIN; TRIGLYCERIDES, BLOOD LEVEL; XANTHOMA.

hypertension BLOOD PRESSURE that remains consistently elevated. Health experts estimate that 25 percent of American adults—about 75 million people—have hypertension, though about half of them do not know it. Hypertension, also called high blood pressure, is a leading cause of STROKE and KIDNEY disease, and a key factor in many heart attacks.

Stroke kills nearly 150,000 Americans each year, making it the third leading cause of death in the United States, and disables about a million others. Yet as many as 80 percent of strokes are preventable through controlling blood pressure. Early diagnosis of hypertension to prevent stroke is a goal of the U.S. preventive health initiative HEALTHY PEOPLE 2010.

Loss of feeling or movement and blurred or dimmed vision, especially on only one side of the body, and difficulty forming or understanding words, are early warning signs of STROKE that require emergency medical evaluation.

Hypertension has numerous effects on the cardiovascular system, and over time alters the function of the HEART as well as the distribution of blood throughout the body. Hypertension in combination with ATHEROSCLEROSIS, the most common form of CARDIOVASCULAR DISEASE (CVD) in the United States, can be particularly damaging or lethal. In combination with DIABETES, hypertension significantly raises the risk for kidney failure and RETINOPATHY of diabetes, in which the tiny blood vessels in the RETINA rupture, causing blindness.

Symptoms and Diagnostic Path

Hypertension has no symptoms, which is why regular blood pressure monitoring is so important. For many people, the first indication of hypertension is stroke or kidney disease, the two leading complications of hypertension. Hypertension may also trigger HEART ATTACK. Occasionally people who have severely elevated blood pressure experience headaches.

Healthy blood pressure is a systolic reading below 120 millimeters of mercury (mm Hg) and a diastolic reading below 80 mm Hg. Persistent readings above these levels for either systolic or diastolic pressure constitute hypertension. Generally the doctor takes several blood pressure readings at different times of the day over a span of time before diagnosing hypertension. A diagnosis of hypertension follows a minimum of three elevated readings. Many people are anxious or nervous when visiting the doctor, sometimes resulting in a phenomenon doctors call "white coat hypertension." An assessment of vital signs, including blood pressure, usually takes place at the start of the health-care visit; when blood pressure is elevated, the doctor may take a measurement again at the end of the visit when the person's anxiety level has dropped.

HYPERTENSION CLASSIFICATIONS

Classification	Systolic	Diastolic
Prehypertension	120–139 mm Hg	80–89 mm Hg
Stage 1 hypertension	140–159 mm Hg	90–99 mm Hg
Stage 2 hypertension	160 mm Hg and above	100 mm Hg and above

Treatment Options and Outlook

Lifestyle modification is the first and the foundational treatment approach for hypertension. Intervention at the prehypertension level can bring blood pressure under control before it becomes a health problem. Overweight or OBESITY causes or exacerbates much hypertension, so often the doctor's first recommendation is weight loss through increased physical activity and changes in eating habits that reduce overall caloric intake. Further dietary modifications often include reducing

sodium consumption, as high amounts of dietary sodium cause the body to maintain fluid. This increases blood volume and, correspondingly, blood pressure. Doctors also recommend reducing dietary fat, especially saturated fat, and cholesterol to reduce the risk for HYPERLIPIDEMIA and atherosclerosis. Atherosclerosis narrows and stiffens the arteries, increasing the resistance blood encounters, and is a significant factor in hypertension.

The mainstay of treatment for hypertension is medication. There are numerous classifications and kinds of drugs that can lower blood pressure through different actions and mechanisms. Often the doctor will combine medications in a multifaceted approach. Many of the medications used to treat hypertension also treat other cardiovascular conditions. Cardiologists often prescribe beta blockers and calcium channel blockers, for example, to treat ARRHYTHMIA, CARDIOMYOPATHY, and HEART FAILURE. Because cardiovascular disease is often a constellation of conditions, this is an effective approach for preventing further cardiovascular disease from developing.

The decision to begin medication for hypertension depends on the blood pressure elevation and other cardiovascular disease or risk factors. Doctors may choose to initiate antihypertensive medication therapy for stage 1 hypertension in people who have multiple cardiovascular risks, yet try three to six months of lifestyle modification for people who have few or no other known cardiovascular risks. Medication needs may change if other health conditions develop or cardiovascular status changes. On the positive side, lifestyle modifications in combination with medication therapy often can reduce or eliminate the need for medication in people who have stage 1 hypertension and occasionally in people who have stage 2 hypertension.

KINDS OF MEDICATIONS TO TREAT HYPERTENSION

angiotensin II receptor blockers (ARBs)	angiotensin-converting enzyme (ACE) inhibitors
beta blockers	calcium channel blockers
diuretics	vasodilators

Risk Factors and Preventive Measures

The leading risk factors for hypertension are age, cigarette smoking, dietary habits, and physical inactivity. Health conditions such as obesity, diabetes, and atherosclerosis further increase the risk for hypertension. Health experts recommend all adults over age 40 undergo annual blood pressure screening, with more frequent screening for people who have increased risk. Daily physical exercise such as walking helps control weight as well as maintain cardiovascular efficiency, reducing risk across the spectrum of cardiovascular disease.

See also CARDIOVASCULAR DISEASE PREVENTION; DIET AND CARDIOVASCULAR HEALTH; LIFESTYLE AND CARDIOVASCULAR HEALTH; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; SMOKING CESSATION.

hypotension Below-normal BLOOD PRESSURE. Hypotension is most often a SIDE EFFECT of medications, a complication of HEART ATTACK, the result of significant BLOOD loss, or a component of cardiovascular SHOCK. Factors that decrease the flow of blood through the body typically result in reduced blood pressure. Idiopathic hypotension (hypotension that exists without apparent cause) often suggests a neurologic cause that reflects damage to the brainstem or HYPOTHALAMUS. STROKE that interrupts blood flow to these parts of the BRAIN may be accountable, interfering with the body's blood pressure regulation mechanisms.

Hypotension is a frequent side effect of many MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE, among them diuretics, antihypertensives (drugs to lower blood pressure), and alpha blockers (drugs to lower blood pressure or treat ARRHYTHMIA). Cardiovascular conditions that reduce CARDIAC OUTPUT (the heart's ability to pump an adequate volume of blood to meet the body's OXYGENATION needs) are common causes of hypotension. Such conditions include severe dilated CARDIOMYOPATHY, advanced HEART FAILURE, bradycardia and other arrhythmias that slow the heart, AORTIC STENOSIS, and unrecognized HEART ATTACK. Hypotension, notably postural hypotension (a sudden drop in blood pressure upon arising), may be a symptom of ADDISON'S DISEASE, an autoimmune disorder that destroys the ADRENAL GLANDS. The adrenal glands produce the key hormones that increase blood pressure, ALDOSTERONE, EPINEPHRINE, and NOREPINEPHRINE.

The most common symptoms of hypotension are lightheadedness and SYNCOPE (fainting), especially when rising from sitting or lying down. The

normal pull of gravity causes blood to temporarily pool in the large veins of the legs. Any lapse between the change of position and the signals that activate the body's blood pressure regulation mechanisms, results in an inadequate blood supply to the brain that causes loss of consciousness. Syncope following meals, called postprandial syncope, also is common, as the body draws an increased blood volume to the gastrointestinal tract to support the functions of digestion. The diagnostic path typically includes review of medications the person is taking as well as blood tests to measure levels of the adrenal hormones, blood electrolytes, and blood composition. Treatment depends on the underlying cause. When the cause is medication, changing the DOSE or switching to a different medication often remedies the hypotension. Neurologic and endocrine causes may require more extensive diagnostic evaluation and comprehensive treatment approaches.

See also ADRENAL INSUFFICIENCY; AUTOIMMUNE DISORDERS; HORMONE; PHEOCHROMOCYTOMA.

I

implantable cardioverter defibrillator (ICD) A small, battery-operated electronic device, similar to a PACEMAKER, that monitors the heart's electrical activity for certain patterns of ARRHYTHMIA and administers a moderate electrical shock when the HEART stays in the pattern beyond the programmed length of time. One or two wires, called leads, extend from the ICD's PULSE generator to the interior of the heart, threaded through a BLOOD vessel during a procedure similar to a CARDIAC CATHETERIZATION. The cardiologist creates a small pocket in the tissues near the shoulder or in the abdomen to implant the pulse generator, a tiny computer. Once placed, the leads and the ICD are permanent. The cardiologist then programs the ICD to maintain the appropriate heart rhythm.

ICD is a treatment option for ventricular tachycardia and VENTRICULAR FIBRILLATION, arrhythmia disorders that affect the ability of the ventricles to contract to expel blood from the heart. Ventricular tachycardia, in which the ventricles contract rapidly but regularly, is exhausting for the heart and does not generate adequate CARDIAC OUTPUT to meet the body's needs. Ventricular fibrillation, in which the ventricles contract rapidly and irregularly, is life-threatening. An ICD can initiate pacing impulses when the heart's rate becomes too slow or a stronger electrical impulse to shock the heart from a harmful to a normal rhythm (CARDIOVERSION). Most people do not feel the pacing impulses though do feel a jolt with cardioversion impulses. People who have ICDs need to be cautious around electrical devices because they generate magnetic fields that can interfere with an ICD's operation and programming.

See also CARDIAC RESYNCHRONIZATION THERAPY (CRT); MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; RADIOFREQUENCY ABLATION.

intermittent claudication PAIN in the lower legs that occurs with physical activity such as walking. Intermittent claudication is the primary symptom of PERIPHERAL VASCULAR DISEASE (PVD), which is ATHEROSCLEROSIS that affects the arteries of the legs. The atherosclerotic accumulations of PVD occlude (block) BLOOD flow through the arteries, limiting their ability to respond to the increased oxygen need of the leg muscles during exercise. The insufficient oxygen causes pain that is typically severe enough to stop the activity. Resting relieves the pain and the person can resume the activity.

People who have intermittent claudication typically develop a pattern of walking and resting that accommodates their symptoms. About 60 percent of people who have intermittent claudication have it in both legs. Cigarette smoking, DIABETES, and lack of physical exercise are the leading causes of PVD and intermittent claudication. The PVD that causes intermittent claudication most often affects the popliteal ARTERY, which branches from the femoral artery and drops behind the knee to supply the lower leg with blood.

The most effective treatment is consistent exercise such as walking. Doctors recommend a progressive approach that begins with walking until pain forces rest, several times every day, and trying to extend the time by a few minutes every week. The regular physical activity conditions the leg muscles, improving the efficiency with which they use oxygen and decreasing oxygen demand. Most people who have PVD and intermittent claudication also take medications to decrease the blood's clotting tendencies, such as ASPIRIN THERAPY or anticoagulation medications such as clopidogrel (Plavix) or warfarin (Coumadin). These methods cannot eliminate intermittent claudication though they can reduce its severity.

See also CARDIOVASCULAR DISEASE PREVENTION; COAGULATION; CORONARY ARTERY DISEASE (CAD); DEEP VEIN THROMBOSIS (DVT); MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; MUSCLE.

intra-aortic balloon pump (IABP) counterpulsation A method to relieve strain on the HEART when there is significant damage to the heart such as after a major HEART ATTACK, in end-stage HEART FAILURE while awaiting HEART TRANSPLANTATION, or in cardiovascular SHOCK. Such circumstances result in the heart being unable to pump enough BLOOD to meet the body's needs. IABP counterpulsation helps pull blood through the AORTA, assisting the left ventricle's pumping efforts.

The cardiologist inserts the IABP on the tip of a catheter during a CARDIAC CATHETERIZATION, threading it through a small incision in a major peripheral ARTERY near the surface of the SKIN, such as the femoral artery in the groin or the brachial artery in the upper arm. The IABP rests in the root of the aorta, its inflated balloon cuff holding it firmly in place. An inner ringlike balloon forms the inside channel of the IABP, inflating and deflating in synchronization with the CARDIAC CYCLE. The channel narrows as the IABP inflates during diastole (filling of the ventricles) and widens as the AIBP deflates during systole (contraction of the ventricles). The effect is to pull blood into the aorta at the same time the left ventricle pumps blood out, easing the amount of pressure necessary to move the blood. A computer closely monitors the heart's electrical patterns to precisely time the inflation and deflation of the IABP's inner balloon.

See also ENHANCED EXTERNAL COUNTERPULSATION (EECP).

ischemic heart disease (IHD) The consequential condition that results when CORONARY ARTERY DISEASE (CAD) and other conditions that affect the heart's blood supply deprive the HEART of oxygen over an extended period of time. Ischemia is the medical term for a temporary interruption of BLOOD flow; in ischemic heart disease (IHD), the interruptions are temporary but recurrent. Cardiac ischemia occurs when the CORONARY ARTERIES are unable to provide the heart with enough blood to meet its oxygen needs. Coronary artery spasm, which often occurs with moderate to advanced CAD, also can generate ischemic episodes.

Ischemia often results in a specific kind of discomfort or PAIN, ANGINA PECTORIS. However, many people who have IHD have what doctors call silent ischemia that causes no symptoms until HEART ATTACK, and sometimes not even then. Silent heart attack can further contribute to the IHD when parts of the heart MUSCLE are no longer functional. IHD may alternately improve and worsen according to the person's activity level, as the heart's oxygen needs increase with activity.

The diagnostic path seeks to identify the underlying condition of the symptoms, which is usually CAD though sometimes ARRHYTHMIA disorders are to blame. Treatment targets the causative condition, and may include ANGIOPLASTY or CORONARY ARTERY BYPASS GRAFT (CABG) as well as medications to regulate the heart's rate and workload. Ischemic heart disease generally improves with these measures.

See also ATHEROSCLEROSIS; CARDIOVASCULAR DISEASE PREVENTION; LIVING WITH CARDIOVASCULAR DISEASE; TRANSMYOCARDIAL LASER REVASCULARIZATION (TMLR).

Kawasaki disease An acute condition affecting children that can weaken the CORONARY ARTERIES and other cardiovascular structures, resulting in HEART ATTACK, ANEURYSM, or permanent damage. Kawasaki disease, also called mucocutaneous LYMPH NODE syndrome, comes on suddenly with RASH, FEVER, CONJUNCTIVITIS, and swollen lymph nodes (LYMPHADENOPATHY). The characteristic symptom that raises suspicion the condition is more than a typical viral INFECTION is the bright red color of the lips and mucous membranes in the MOUTH. After about five days the palms of the hands and soles of the feet also become bright red. The child appears, and is, very ill. The acute phase of the disease runs about three weeks. The diagnostic path is primarily clinical; there are no definitive tests for Kawasaki disease.

Treatment during the acute phase includes efforts to keep the child comfortable as well as administering high-DOSE aspirin. Aspirin, not usually given to children who have fevers because of the risk for REYE'S SYNDROME, is the treatment of choice for Kawasaki disease because it not only reduces FEVER but also reduces cardiovascular INFLAMMATION and has antiplatelet action that helps prevent blood clots from forming. These effects lower the likelihood of cardiovascular damage or crisis. Intravenous IMMUNOGLOBULIN, which delivers generalized antibodies that aid the body's IMMUNE RESPONSE, given early in the course of the disease seems to mitigate symptoms in some children.

Sometimes cardiovascular symptoms manifest during the disease's acute phase, though typically it is months to years later that problems become apparent. Doctors recommend cardiovascular assessment, including ELECTROCARDIOGRAM (ECG) and ECHOCARDIOGRAM, for children at the time of diagnosis. Detected cardiovascular changes require regular followup, with treatment as necessary. The most serious long-term consequences of Kawasaki disease are aneurysms of the coronary arteries that cause heart attack. In some children, inflammation attacks the heart valves, resulting in VALVULAR HEART DISEASE that requires ongoing medical attention and sometimes heart valve replacement in adulthood.

Doctors believe an infectious agent, such as a VIRUS, likely causes Kawasaki disease though as yet researchers have been unable to isolate it. Though occasionally there appear to be clusters of Kawasaki disease, the condition does not appear to be contagious through contact among family members and close contacts. Children under five years of age are most likely to develop Kawasaki disease. Children who have had Kawasaki disease rarely get it again.

See also ANTIBODY; SCARLET FEVER; TOXIC SHOCK SYNDROME.

L

left ventricular ejection fraction (LVEF) The percent of BLOOD a full left ventricle pumps into the AORTA with each CARDIAC CYCLE. LVEF provides an assessment of cardiovascular limitations resulting from damage to the HEART such as by MYOCARDIAL INFARCTION or HEART FAILURE. Normal LVEF is 55 percent; LVEF below 35 percent indicates severe heart failure. Because it is not possible to directly measure the volume of blood the left ventricle pumps, cardiologists use indirect methods to calculate the LVEF. Among these methods are ECHOCARDIOGRAM with Doppler ULTRASOUND, radionuclide scans, and MAGNETIC RESONANCE IMAGING (MRI), all of which allow the cardiologist to mathematically determine the volume of the ventricle and visualize the flow of blood through the heart. LVEF is one method to monitor the progression of a degenerative cardiovascular condition such as heart failure as a criterion for HEART TRANSPLANTATION.

See also CARDIAC CAPACITY; CARDIAC OUTPUT.

lifestyle and cardiovascular health The variables of daily living and the effects they have on the health of the HEART and BLOOD vessels. Health experts estimate that lifestyle modifications alone could eliminate 90 percent or more of acquired CARDIOVASCULAR DISEASE (CVD). Given that 60 million Americans currently have at least one form of cardiovascular disease, the potential impact of such a reduction on LIFE EXPECTANCY as well as QUALITY OF LIFE is overwhelming. The three lifestyle factors that most significantly influence cardiovascular health are cigarette smoking, dietary habits, and physical activity.

Cigarette Smoking

NICOTINE, the active ingredient in cigarette smoke, is a potent vasoconstrictor and cardiovascular stimulant. Before a smoker finishes the first inhalation from a cigarette, nicotine is already surging through the bloodstream. It causes blood vessels throughout the body to stiffen and narrow, raising BLOOD PRESSURE. It raises the HEART RATE, further increasing blood pressure as well as the heart's workload. Simultaneously, other substances in cigarette smoke interfere with the OXYGEN–CARBON DIOXIDE EXCHANGE in the LUNGS, reducing the amount of oxygen the blood carries into the blood circulation. As smoking continues over time, nicotine causes physical changes in the cells of the ARTERY walls, reducing their ability to contract and relax. Blood pressure elevation may become permanent (HYPERTENSION), and the arteries are more susceptible to ATHEROSCLEROTIC PLAQUE. With SMOKING CESSATION much of the arterial function returns. Hypertension may improve though ATHEROSCLEROSIS, including CORONARY ARTERY DISEASE (CAD) and PERIPHERAL VASCULAR DISEASE (PVD), remains.

Dietary Habits

The foods and the quantities of them that a person eats significantly influence blood levels of cholesterol and triglycerides. A diet high in fruits, vegetables, and whole grain products provides a rich source of vitamins, antioxidants, and fiber that help regulate these lipids. This is important because elevated blood lipids (HYPERLIPIDEMIA) form the basis of atherosclerosis and the conditions that result, notably hypertension, CAD, and PVD. These nutrients also help the body tissues, including those of the cardiovascular system, to function efficiently. Nutritious eating further helps regulate the body's GLUCOSE–INSULIN balance, important from a cardiovascular perspective because insulin plays a key role in the kinds and amounts of cho-

lesterol and lipoproteins the LIVER manufactures. Insulin is also a key player in type 2 DIABETES, which is another risk factor for cardiovascular disease. Eating too much of any kind of food, however, results in increased body weight. OBESITY is another risk factor for numerous forms of CVD, notably hypertension and atherosclerosis. For many people a weight loss of 10 pounds can decrease systolic blood pressure by 10 millimeters of mercury (mm Hg) and lower CHOLESTEROL BLOOD LEVELS by 5 to 10 percent.

Physical Exercise

Daily physical activity is emerging as perhaps the single-most important lifestyle factor in regard to cardiovascular health and perhaps health overall. Exercise affects cellular METABOLISM in numerous ways. Cardiovascularly, exercise improves the efficiency with which cells use oxygen, lowering demand on the heart. AEROBIC EXERCISE increases LUNG CAPACITY, putting more oxygen into the blood with each breath. Exercise also increases insulin sensitivity, improving cholesterol ratios as well as glucose efficiency. Walking aids the lower extremities in moving blood back to the heart, with the skeletal muscles massaging and supporting the veins that must work against gravity to accomplish this task.

Lifestyle Modifications

Health experts agree that while the greatest cardiovascular benefits come from lifelong lifestyle habits that support cardiovascular health, it is never too late to make changes that improve cardiovascular status. Even when cardiovascular disease exists, doing lifestyle modifications such as nutritious EATING HABITS, daily physical exercise, WEIGHT LOSS AND WEIGHT MANAGEMENT, and SMOKING CESSATION can mitigate symptoms and allow a more acceptable quality of life.

See also CARDIOVASCULAR DISEASE PREVENTION; DIET AND CARDIOVASCULAR HEALTH; DIET AND HEALTH; EXERCISE AND HEALTH; HEALTH RISK FACTORS; HEALTHY PEOPLE 2010; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; SMOKING AND CARDIOVASCULAR DISEASE.

living with cardiovascular disease More than 70 million Americans—nearly 35 percent of the U.S. population—live with some form of diagnosed CARDIOVASCULAR DISEASE (CVD). Many of them continue in the jobs and leisure activities they have always enjoyed, due in large part to advances in technology, surgery, and drugs that allow early diagnosis, prompt intervention, and successful treatment. Others—about 10 million—find their lives entirely changed by permanent disability. STROKE alone disables nearly a million Americans each year. Some people see their cardiovascular conditions as opportunities to improve their health and QUALITY OF LIFE, and some people see them as limitations. Living with CVD has physical and emotional dimensions that reach into nearly every aspect of life, from work and career to relationship and family.

Physical Dimensions

About 10 million Americans live with some degree of permanent disability as a result of CVD that limits their abilities to work and participate in activities they enjoy. One in three people who has a stroke experiences residual complications ranging from memory and cognitive disturbances to PARALYSIS. Half of people who have heart attacks experience compromised cardiovascular function, some of which is short term and improves over time, and some of which is long term and does not get much better with time. These changes may require adaptive accommodations in the home and the workplace. CARDIAC REHABILITATION programs help people recover to the best level possible, teaching new methods for managing lifestyle tasks and establishing individual recovery goals and the steps to reach them.

Emotional Dimensions

People who experience heart attack and other cardiovascular crises find themselves confronting their own mortality in ways that can be disconcerting and frightening. Some people experience renewed appreciation for life and its daily details. Some people turn to faith, either in gratitude or in anger. Some people flail about emotionally, suddenly unsure of life's purpose. Family members may not understand or may themselves find the close call a frightening experience. Feelings and emotions are as much a part of managing cardiovascular conditions as are medications and operations. Medical centers and hospitals that provide

cardiovascular care typically sponsor support groups where people can share their worries and fears.

Outlook

In the course of 40 years—the span of a generation—cardiovascular disease shifted from harbinger of restricted living and early death to a plethora of treatment options. For many people, living with cardiovascular disease is little different from living without cardiovascular disease. Operations, medications, and lifestyle interventions can mitigate many forms of cardiovascular disease. With the intensified focus on preventive measures and interventions, the generation born at the turn of the 21st century could be the first that does not have the experience of living with cardiovascular disease.

See also CARDIOVASCULAR DISEASE PREVENTION; LIFESTYLE AND CARDIOVASCULAR HEALTH; RISK FACTORS FOR CARDIOVASCULAR DISEASE.

long QT syndrome (LQTS) An ARRHYTHMIA disorder in which an electrical conduction defect in the HEART results in delayed repolarization of myocardial cells. Repolarization is the process by which myocardial cells restore themselves to receive another electrical impulse. With LQTS, the myocardial cells hold a positive charge much longer than normal, preventing the heart from recharging for the next CARDIAC CYCLE. Most LQTS is hereditary, and researchers have isolated a number of GENE mutations that affect the heart's ion channels (conductive pathways), usually potassium channels though sometimes sodium channels. The condition can also develop as a consequence of STROKE or as a medication SIDE EFFECT, notably with antiarrhythmia and ANTIDEPRESSANT MEDICATIONS though numerous drugs affect the QT interval.

The points Q and T on the ELECTROCARDIOGRAM (ECG) identify polarization or discharge of electrical activity (the Q wave) and repolarization (the T wave). Doctors call the amount of time it takes for this phase to complete the QT interval. The longer the QT interval, the greater the risk for a dangerous arrhythmia called TORSADE DE POINTES, a form of highly unstable ventricular tachycardia (rapid though regular contractions of the ventricles, typically exceeding 100 contractions a minute). Torsade de pointes can quickly lead to VENTRICULAR FIBRILLATION, in which the ventricular contractions are rapid, irregular, and nonfunctional. Ventricular fibrillation quickly becomes life-threatening and may require emergency DEFIBRILLATION. LQTS is a common cause of SUDDEN CARDIAC DEATH in young people who are apparently healthy.

Symptoms and Diagnostic Path

Often, people who have LQTS do not have symptoms, and doctors detect the condition during ECG done for other reasons. The most common symptom that does occur is unexplained syncope (fainting), especially with intense exercise or emotional response (such as anger or fear). ECG generally provides the diagnosis, though the cardiologist may do an exercise STRESS TEST to evaluate the heart's electrical response with increased physical activity.

Treatment Options and Outlook

The standard medical treatment for LQTS is a beta blocker medication, which helps slow and stabilize the HEART RATE. The beta blockers most commonly prescribed for LQTS are propanolol (Inderal), metoprolol (Lopressor or Toprol), nadolol (Corgard), and atenolol (Tenormin). Beta blockers control LQTS in about 70 percent of people who have the condition. When medications fail to prevent arrhythmias, the next level of treatment is an IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD), an electronic device similar to a PACEMAKER. The ICD monitors the heart's rhythm and can deliver an electrical shock to return the heart to a normal rhythm should dangerous arrhythmias occur.

Because a prolonged QT interval is most likely to occur during intense physical exercise that puts high demand on the heart LQTS may require lifestyle modifications, especially for people who participate in competitive sports. Most people are able to enjoy recreational athletic and physical activities, however.

Risk Factors and Preventive Measures

Gene mutations establish the foundation for LQTS, probably even in secondary LQTS (LQTS

that results as a side effect of medication or other events). Family history of LQTS or sudden cardiac death is an important diagnostic clue. When LQTS is secondary, removing the cause often ends the conductive irregularities. There are no known preventive measures for primary LQTS. Treatment often controls symptoms and prevents life-threatening arrhythmia.

See also CARDIAC ARREST; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; TAMPONADE, CARDIAC.

medications to treat cardiovascular disease Drugs that alter the function of the HEART or the BLOOD vessels. Plants provided the earliest forms of DRUG therapy for heart problems. Healers in ancient Egypt and Greece brewed teas of foxglove leaves, the source of digitalis, to slow a rapid heartbeat and strengthen a weakened heart. By the 17th century physicians were using a relatively standardized formulation of powdered foxglove to treat congestive HEART FAILURE. Foxglove leaves remain the source from which laboratories extract digitalis to manufacture digoxin and digitoxin, the digitalis-based medications that remain in use today. Quinidine, a medication to treat ARRHYTHMIA (irregular heartbeat), derives from the bark of the South American *Cinchona ledgeriana* tree (also the original source of the antimalarial drug quinine). Scientists isolated quinidine as an extract to treat ATRIAL FIBRILLATION in 1918. *Rauwolfia serpentina* was a staple in the PHARMACOPOEIA of healers in ancient India, who used its dried roots to lower BLOOD PRESSURE. The antihypertensive medication reserpine, which debuted in the 1950s, contains *Rauwolfia* alkaloid extracts. Today medications are the mainstay of treatment for most forms of CARDIOVASCULAR DISEASE (CVD), though most are synthetic formulations that come from the laboratory.

Cardiovascular disease often involves multiple, interrelated components. HYPERTENSION (high blood pressure) often arises from underlying ATHEROSCLEROSIS, the most common cardiovascular disease. CORONARY ARTERY DISEASE (CAD), a manifestation of atherosclerosis that affects the CORONARY ARTERIES supplying the heart, may generate arrhythmias and ANGINA PECTORIS. Heart failure typically features numerous symptoms arising from a constellation of cardiovascular dysfunctions. The recent direction of research has correspondingly produced medications that treat the constellation, not just a single symptom. A calcium channel blocker, a classification of medication that debuted in the 1990s, dilates peripheral arteries, and slows the HEART RATE; these actions lower blood pressure, regulate the heart's rhythm, and strengthen the heart's pumping action. Combining medications often produces more effective results. For example, the cardiologist may also prescribe a diuretic to extract additional fluid from the body, which lowers blood volume and thus blood pressure, which in turn relieves the heart's workload to reduce heart failure. The combination of the diuretic and the calcium channel blocker may restore nearly normal cardiovascular function.

People respond differently to cardiovascular drugs, even when they have the same diagnoses. It may take a trial and error period to find the right medication or combination of medications for each individual. Cardiovascular medications may interact or interfere with each other, with medications for other health conditions, with herbal preparations, and with certain foods. For example, grapefruit (whole fruit or juice) interferes with the actions of calcium channel blockers, statin lipid-lowering medications, digoxin, potassium channel blockers, and warfarin. The herb GOLDENSEAL, taken to enhance immune function, elevates blood pressure and interacts with antihypertensive medications. Dark green leafy vegetables contain VITAMIN K, which increases clotting and interferes with anticoagulant medications.

Most medications to treat cardiovascular conditions have the potential for side effects, some of which may be life-threatening. Sodium channel and potassium channel blockers, digoxin, warfarin, and heparin all are NARROW THERAPEUTIC INDEX (NTI) drugs, for which the margin between

helpful and harmful is exceedingly thin. These drugs have the potential to create life-threatening arrhythmias. Other cardiovascular medications may cause symptoms such as COUGH, HEADACHE, ERECTILE DYSFUNCTION, tiredness, CONSTIPATION, dizziness, flushing, and edema (swelling, particularly of the ankles and wrists). It is important for people to know what side effects are possible with they medications they are taking and to notify the doctor if any of them occur. Though some side effects are common to all of the drugs within a classification, sometimes switching to a different medication within the same classification eliminates the troublesome side effect.

ACE Inhibitors

Angiotensin-converting enzyme (ACE) inhibitors block the action of angiotensin-converting enzyme (ACE). Angiotensin II is a potent vasoconstrictor that raises blood pressure. Blocking the conversion of its precursor, angiotensin I (angiotensinogen), prevents these events and lowers blood pressure. ACE inhibitors also have a mild to moderate diuretic effect, further lowering blood pressure by reducing blood volume.

Pregnant women should not take ACE inhibitors during the second and third trimesters of PREGNANCY, as these drugs may cause harm or death to the fetus.

Doctors prescribe ACE inhibitors as first-line treatment, usually in combination with diuretics, to treat hypertension and heart failure and to reduce the risk of subsequent heart attacks after an initial heart attack. Some ACE inhibitor products combine an ACE inhibitor with a diuretic.

COMMON ACE INHIBITORS

benazepril (Lotensin)	captopril (Capoten)
enalapril (Vasotec)	fosinopril (Monopril)
lisinopril (Prinivil, Zestril)	moexipril (Univasc)
perindopril (Aceon)	quinapril (Accupril
ramipril (Aceon (Altace)	trandolapril (Mavik)

Among the common side effects are HEADACHE, gastrointestinal upset, dizziness, SKIN RASH or skin sensitivity to sunlight, and fatigue. ACE inhibitors have a propensity to cause a dry, nonproductive cough; though annoying, the cough is benign and typically goes away within two months of stopping the medication.

Adenosine

Adenosine is an intravenously administered medication that momentarily interrupts the flow of the heart's electrical pacing signals, creating an "electrical short" of sorts that very briefly stops the heart. It is a treatment for PAROXYSMAL ATRIAL TACHYCARDIA (PAT), also called paroxysmal supraventricular tachycardia (PSVT), that converts the heart to normal sinus rhythm. Sometimes cardiologists refer to this treatment as chemical or pharmaceutical CARDIOVERSION. Adenosine is available in the United States as the brand name product Adenocard. The effects of adenosine last only one to two minutes. Side effects may include headache, lightheadedness, NAUSEA, and shortness of breath (DYSPNEA). Adenosine also may trigger angina pectoris in people who have CAD.

Alpha Blockers

Alpha blockers, also called alpha adrenergic antagonist medications, block alpha receptors in the cells from binding with EPINEPHRINE (also called adrenaline). These drugs were among the first generation of antihypertensive medications, though beta blockers and other antihypertensives have generally replaced them. Alpha blockers relax smooth MUSCLE, including that in the walls of the arteries to produce arterial dilation. This reduces the resistance for the flow of blood, lowering blood pressure. The most common cardiovascular use of alpha blockers is to treat hypertension that arises from PHEOCHROMOCYTOMA. This endocrine tumor secretes the hormones epinephrine and NOREPINEPHRINE, causing extreme spikes in blood pressure.

Alpha blockers are not a first-line treatment approach for general hypertension because their effects are widely systemic and because their long-term use increases the risk for heart failure. Alpha blockers affect other sites of smooth muscle tissue throughout the body, such as in the gastrointestinal tract, acting to slow peristalsis, and in the genitourinary system, causing URINARY INCONTINENCE and ERECTILE DYSFUNCTION. Other side effects may include dizziness and SYNCOPE (fainting). Some alpha blockers also block beta receptors.

COMMON ALPHA BLOCKERS

clonidine (Catapres)	doxazosin (Cardura)
guanabenz (Wytensin)	guanfacine (Tenex)
labetalol (Normodyne)	methyldopa (Aldomet)
phenoxybenzamine (Dibenzyline)	prazosin (Minipress)
terazosin (Hytrin)	

Angiotensin II Receptor Blockers (ARBs)

Angiotensin II receptor blockers, also called angiotensin II receptor antagonists or ARBs, prevent the enzyme angiotensin II from binding with cells the walls of the arteries. Angiotensin II is a powerful endogenous vasoconstrictor (substance the body makes to narrow the blood vessels) that raises blood pressure. Preventing its actions relaxes and dilates the arteries, reducing the resistance blood encounters flowing through them and lowering blood pressure.

Pregnant women should not take angiotensin II receptor blockers (ARBs) during the second and third trimesters of PREGNANCY, as these drugs may cause harm or death to the fetus.

ARBs may be the first-line choice to treat hypertension, depending on the person's overall health profile and other medications. ARBs do not cause the cough and other side effects that can be troublesome with ACE inhibitors, though they do put more strain on the kidneys. The most common side effect with ARBs is headache, especially with losartan. Other side effects, though uncommon, may include anxiety, fatigue, and gastrointestinal upset.

COMMON ANGIOTENSIN II RECEPTOR BLOCKERS

candesartan (Atacand)	eprosartan (Teveten)
irbesartan (Avapro)	losartan (Cozaar)
olmesartan medoxomil (Benicar)	tasosartan (Verdia)
telmisartan (Micardis)	valsartan (Diovan)

Anticoagulants

People commonly refer to anticoagulant drugs as "blood thinners" though this is somewhat of a misnomer. The first stage of clotting, which anticoagulants delay, is a thickening of the blood as CLOTTING FACTORS begin causing cells to stick together. Anticoagulants prevent the body from processing vitamin K, which interferes with the blood's ability to activate clotting factors. Heparin, low molecular weight heparin (LMWH), and fondaparinux are injectable anticoagulants that are relatively short-acting though have cumulative effects when administered for extended periods of time. Surgeons use anticoagulants to completely suppress the blood's clotting ability during operations that require CARDIOPULMONARY BYPASS. Warfarin (Coumadin) is currently the only oral anticoagulant available, though research continues to search for alternatives. Anticoagulants are NTI drugs that require continual monitoring to maintain therapeutic levels.

Women who are pregnant or planning to become pregnant should not take warfarin, as it can cause birth defects (highest risk during first trimester).

Doctors prescribe anticoagulant medications to prevent blood clots from forming, typically to prevent DEEP VEIN THROMBOSIS (DVT) and PULMONARY EMBOLISM in PERIPHERAL VASCULAR DISEASE (PVD) with INTERMITTENT CLAUDICATION, and to prevent heart attack and stroke. Anticoagulants cannot dissolve clots that already exist (though thrombolytic agents can). The most significant side effect is excessive bleeding. Anticoagulants can interact with numerous medications. Foods high in vitamin K (such as dark green leafy vegetables) may increase the blood's clotting capability.

COMMON ANTICOAGULANTS

heparin	fondaparinux (Arixtra)
warfarin (Coumadin)	
LMWHs:	
ardeparin (Normiflo)	dalteparin (Fragmin)
enoxaparin (Lovenox)	nadroparin (Fraxiparine)
reviparin (Clivarine)	tinzaparin (Innohep)

Antiplatelet Agents

Antiplatelet agents also interfere with the blood's ability to clot by blocking platelets, the cells that initiate clotting, from aggregating or sticking together. PLATELET AGGREGATION sets in motion the sequence of chemical interactions that activate clotting factors; blocking PLATELET aggregation

delays the start of the clotting process. Antiplatelet agents often are part of an ANTICOAGULATION THERAPY regimen, in combination with anticoagulant medications.

The most commonly used antiplatelet agent is low-dose aspirin, which health experts recommend for people who have increased risk for cardiovascular disease or who have already had heart attack or ischemic stroke. Like anticoagulants, antiplatelet agents require close monitoring to maintain therapeutic levels. Three antiplatelet agents are injectable only—abciximab (Rheopro), eptifibatide (Integrilin), and tirofiban (Aggrastat)—which doctors use during ANGIOPLASTY and sometimes other CARDIAC CATHETERIZATION procedures. The oral antiplatelet agent cilostazol (Pletal) also acts to dilate the blood vessels, so doctors often prescribe it to treat intermittent claudication.

Doctors typically prescribe antiplatelet agents to prevent clots from forming in people who have PVD, CAD, valvular heart disease, prosthetic heart valves, PACEMAKER or IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD), or who have had heart attack, stroke, or certain kinds of heart surgery. The most significant side effect of antiplatelet agents is excessive bleeding. Over-the-counter NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen, and the herbal product ginkgo biloba, also have mild antiplatelet activity; it is important to check with the doctor or pharmacist before taking them with prescribed antiplatelet agents.

COMMON ANTIPLATELET AGENTS

abciximab (Rheopro)	cilostazol (Pletal)
clopidogrel (Plavix)	dipyridamole (Persantine)
eptifibatide (Integrilin)	sulfinpyrazone (Anturane)
ticlopidine (Ticlid)	tirofiban (Aggrastat)

Beta Blockers

Beta blockers, also called beta adrenergic antagonist medications or class II antiarrhythmics, block beta receptors in the cells from binding with epinephrine. Beta receptors are specific to the arteries and MYOCARDIUM, so the actions of beta blockers are selective and specific to these sites. In the heart, beta blockers slow the conduction of electrical impulses, which slows the heart rate and reduces the amount of blood the heart pumps (CARDIAC OUTPUT). These effects result in lowered blood pressure and also reduced cardiac workload, which relieves angina pectoris. In the arteries, beta blockers cause smooth muscle tissue to relax, which dilates the arteries to decrease the resistance blood encounters to lower blood pressure. Most beta blocker medications thus do not have the systemic or generalized effects of alpha blockers, though a few of the beta blockers (notably propanolol and sotalol) also have some alpha antagonist activity as well and may have mild systemic effects.

There are two kinds of beta receptors, beta 1 and beta 2. Muscle cells in the myocardium and NERVE cells that regulate heart rate contain primarily beta 1 receptors. Peripheral arteries and arterioles contain primarily beta 2 receptors. Different beta blocker drugs target either beta 1 or beta 2 receptors. The smooth muscle cells in the airways also contain beta 2 receptors, so beta blockers that affect beta 2 receptors in the blood vessels also affect the airways. Medications to treat ASTHMA may interact with beta blockers taken to treat cardiovascular conditions. Beta blockers prescribed for other conditions such as asthma, BENIGN PROSTATIC HYPERTROPHY (BPH), migraine headaches, GLAUCOMA, and essential tremor may also affect cardiovascular function.

Do not suddenly stop taking a beta blocker, as doing so may cause intensified ANGINA PECTORIS and increased risk for HEART ATTACK.

Beta blockers are the "workhorse" drugs in cardiology, treating a broad spectrum of cardiovascular conditions. Doctors prescribe beta blockers to treat hypertension, heart failure (especially congestive heart failure), atrial fibrillation, mild to moderate ventricular tachycardia, CARDIOMYOPATHY, angina pectoris, and to improve survival following heart attack. The most common side effects are fatigue and sleepiness, which generally improve with taking the medication over time. Beta blockers may cause erectile dysfunction in men and diminished sexual response in women. CAFFEINE and antihistamines (such as in cold and allergy products) intensify, and ALCOHOL diminishes, the effects of beta blockers. Beta blockers may interfere with the actions of oral ANTIDIABETES MEDICATIONS.

COMMON BETA BLOCKERS

acebutolol (Sectral)	atenolol (Tenormin)
betaxolol (Kerlone)	bisoprolol (Zebeta)
carteolol (Cartrol)	esmolol (Brevibloc)
metoprolol (Lopressor, Toprol)	nadolol (Corgard)
penbutolol (Levatol)	pindolol (Visken)
propranolol (Inderal)	timolol (Blocadren)

Calcium Channel Blockers

Calcium channel blockers, also called calcium channel antagonists, limit the amount of calcium that enters contractile cells. Two of the commonly prescribed calcium channel blockers act nearly exclusively on the heart (myocardial cells), diltiazem and verapamil. Cardiologists prescribe these drugs, also identified as class IV antiarrhythmics, to treat atrial fibrillation, PAT, hypertrophic cardiomyopathy, and angina pectoris. The other calcium channel blockers, sometimes called dihydropyridine calcium channel blockers, act primarily on the peripheral arteries, causing them to relax and dilate. This lowers resistance for blood flow and reduces blood pressure. Cardiologists prescribe these calcium channel blockers to treat hypertension, angina pectoris without arrhythmia, and RAYNAUD'S SYNDROME. Doctors use nimodipine following stroke to reduce the risk of arterial spasm and resulting HEMORRHAGE, as it affects primarily the arteries in the BRAIN.

Women who are pregnant or planning to become pregnant should not take calcium channel blockers, as these drugs can cause serious birth defects and STILLBIRTH.

COMMON CALCIUM CHANNEL BLOCKERS

amlodipine (Norvasc, Lotrel)	diltiazem (Cardizem, Cartia, Dilacor, Diltia, Tiazac)
felodipine (plendil)	nicardipine (Cardene)
isradipine (DynaCirx)	nimodipine (Nimotop)
nifedipine (Adalat, Procardia)	nisoldipine (Sular)
verapamil (Calan, Covera, Isoptin, Verelan)	

Side effects that may occur when taking calcium channel blockers include headache, gastrointestinal upset, fatigue, and peripheral edema. Most side effects retreat after a few weeks of taking the medication. Grapefruit and grapefruit juice interfere with most calcium channel blockers, preventing them from working properly.

Diuretics

People commonly refer to diuretic medications as "water pills" because they draw extra fluid from the body, increasing urination. The purpose is to reduce the volume of blood, which lowers blood pressure. Diuretics also help prevent edema (fluid accumulations in body tissues) such as may occur with heart failure. Doctors often prescribe diuretics in combination with other medications. There are four classifications of diuretic medications, defined by the drug's mechanism of action: ALDOSTERONE blockers, loop diuretics, potassium-sparing diuretics, and thiazides.

Aldosterone blockers Aldosterone blockers act by restricting adrenal gland production of the HORMONE aldosterone, which increases the amount of sodium the KIDNEYS withdraw from the blood. They affect the RENIN-angiotensin-aldosterone (RAA) hormonal system, one of the body's primary blood pressure regulatory systems. Though aldosterone blockers prevent the kidneys from reabsorbing sodium, they decrease the loss of potassium so they are also designated as "potassium-sparing." However, new understanding emerged in the early 2000s about other effects aldosterone has on the heart, particularly following heart attack and in heart failure and with respect to the RAA hormonal system, that have caused doctors to view aldosterone blockers as a separate category of diuretic.

The two aldosterone blockers available in the United States are eplerenone (Inspra) and spironolactone (Aldactone).

Loop diuretics Loop diuretics act on a site within the glomerular structure of the kidney called the loop of Henle, which regulates sodium reabsorption. Loop diuretics cause the kidneys to pass more sodium, and consequentially more water, into the urine, and are the most potent of the diuretic drugs. As the loop of Henle also plays a role in potassium regulation, loop diuretics also decrease potassium reabsorption and can result in potassium depletion. Doctors may also prescribe potassium supplementation to offset this effect. The most common side effect of loop diuretics is

headache. Loop diuretics also can damage the structures of the inner EAR, resulting in temporary or permanent HEARING LOSS.

COMMON LOOP DIURETICS

bumetanide (Bumex)	ethacrynic acid (Edecrin)
furosemide (Lasix, Myrosemide)	torsemide (Demadex)

Potassium-sparing diuretics These drugs prevent the kidneys from withholding sodium, the electrolyte most responsible for fluid retention, though allow the kidneys to pull potassium from the blood. They are the least potent of the diuretic drugs, acting on other sites in the glomeruli that regulate specifically sodium reabsorption. The two potassium-sparing diuretics available in the United States are amiloride (Midamor) and triamterene (Dyrenium). The aldosterone blockers eplerenone and spironolactone are also potassium sparing.

Thiazide diuretics The thiazide diuretics are the first line of therapy for hypertension and heart failure, often in combination with other cardiovascular medications. Their actions are more moderate than those of the loop diuretics, creating less of a risk for potassium depletion though such risk still exists. There are numerous thiazide diuretics, only some of which doctors prescribe for cardiovascular conditions. Because thiazides are so commonly used with other medications, there are also numerous formulations that incorporate a thiazide with another cardiovascular drug.

COMMON THIAZIDE DIURETICS

chlorothiazide (Diuril, Diurigen)
chlorthalidone (Hygroton, Thalitone)
hydrochlorothiazide (Ezide, Esidrix, HCTZ, Hydro-Chlor, Hydro-D, HydroDIURIL, Microzide, Oretic)
hydroflumethiazide (Diucardin, Saluron)
methyclothiazide (Aquatensen, Enduron)
metolazone (Diulo, Mykrox, Zaroxolyn)
polythiazide (Renese)
quinethazone (Hydromox)
trichlormethiazide (Metahydrin, Naqua, Trichlorex)

Inotropics

Inotropic drugs draw more calcium into myocardial cells, intensifying their contractility (the force with which they contract) and increasing the heart's effectiveness while decreasing the effort required. Inotropic drugs administered intravenously during cardiovascular emergency include dopamine, dobutamine, and milrinone; these drugs give the heart a "jolt" to help it pull out of CARDIAC ARREST. Digoxin (short-acting) and digitoxin (long-acting), forms of digitalis, are the inotropic medications for chronic or extended oral therapy. Though once the cornerstone of therapy for heart failure (notably congestive heart failure), digoxin has a very narrow therapeutic index, making toxicity a worrisome concern. Digoxin interacts with numerous other medications including those that more effectively treat heart failure, and the heart becomes dependent on it.

Digoxin also acts to slow the number of electrical impulses that cross the ATRIOVENTRICULAR (AV) NODE, slowing and regulating the contractions of the myocardial cells. Cardiologists may prescribe digoxin to treat atrial fibrillation. The most common brand name digoxin product in the United States is Lanoxin.

Lipid-Lowering

Lipid-lowering medications reduce blood levels of cholesterol and triglycerides, lowering the risk for atherosclerosis and its related conditions CAD and PVD. There are four classifications of lipid-lowering medications, each with a different mechanism of action: BILE acid sequestrants, fibrates, statins, and selective cholesterol absorption inhibitors. As well, niacin acts to block cholesterol and lipoprotein synthesis in the LIVER.

Bile acid sequestrants The bile acid sequestrants were the first cholesterol-lowering medications to become available. They work by binding with bile in the gastrointestinal tract, preventing the body from reabsorbing cholesterol the bile contains. Bile acid sequestrants can reduce low-density lipoprotein cholesterol (LDL-C) by about 20 percent and total cholesterol by 5 to 10 percent. These medications come as powders to mix with juices or foods such as applesauce, and commonly cause gastrointestinal distress. Bile acid sequestrants interact with numerous medications, including beta blockers, diuretics, and the anticoagulant warfarin.

COMMON BILE ACID SEQUESTRANTS

cholestyramine (Questran, Prevalite)	colesevelam (WelChol)
	colestipol (Colestid)

Fibrates The fibrates work by blocking the liver's production of LDL and VLDL (very low-density lipoprotein), the carriers for triglycerides. However, fibrates do not lower LDL-C or VLDL-C in the blood. Rather, they primarily reduce triglycerides though also raise high-density lipoprotein cholesterol (HDL-C), the "good" cholesterol. The most common side effect of fibrates is gastrointestinal distress, which usually disappears after taking the medication for a few weeks.

COMMON FIBRATES

clofibrate (Atromid-S)	fenofibrate (Tricor)
gemfibrozil (Lopid)	

Statins Statins—or 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors—are the most commonly prescribed lipid-lowering medications. They work by blocking the action of HMG-CoA reductase, an enzyme necessary for the liver to synthesize cholesterol. Statins can lower blood LDL cholesterol by as much as 35 percent in just three to six weeks, making them very effective at quickly lowering the risk for atherosclerosis-related cardiovascular events. Statins reduce the risk for the progression of CAD, which could improve heart function after heart attack and are part of the standard medication regimen after heart attack and HEART TRANSPLANTATION. Common side effects of statins include gastrointestinal distress, fatigue, headache, and sleep disturbances.

COMMON STATINS

atorvastatin (Lipitor)	fluvastatin (Lescol)
lovastatin (Mevacor)	pravastatin (Pravachol)
simvastatin (Zocor)	

Selective cholesterol absorption inhibitors The selective cholesterol absorption inhibitors block the gastrointestinal tract from absorbing dietary cholesterol, limiting the cholesterol that enters the bloodstream. Ezetimibe (Zetia) is currently the only drug in this classification that is available in the United States. Doctors often prescribe ezetimibe in combination with statin medications for the most effective lipid-lowering effect.

Potassium Channel Blockers

Potassium channel blockers, also called potassium channel antagonists or class III antiarrhythmics, limit the amount of potassium, a key electrolyte (chemical that can carry an electrical impulse), that can enter myocardial cells. This limitation restricts the flow and pattern of electrical impulses through the heart in very specific ways. Cardiologists prescribe potassium channel blockers to treat atrial fibrillation that does not respond to other medications and to treat atrial tachycardia. These drugs interact with numerous medications, including those prescribed to treat cardiovascular conditions (notably digoxin and warfarin) and to treat other health conditions such as DIABETES. Amiodarone increases sensitivity to ultraviolet light, which can result in severe SUNBURN even through clothing. Potassium channel blockers have numerous serious side effects including life-threatening or fatal arrhythmias and TORSADE DE POINTES, a highly unstable form of ventricular tachycardia.

COMMON POTASSIUM CHANNEL BLOCKERS

amiodarone (Cordarone)	dofetilide (Tikosyn)
ibutilide (Corvert)	

Sodium Channel Blockers

Sodium channel blockers, also called sodium channel antagonists or class I antiarrhythmics, limit the amount of sodium that enters myocardial cells. This limitation restricts the flow and pattern of electrical impulses through the heart in very specific ways that differ from the actions of potassium channel blockers. Because sodium is critical for myocardial contraction, restricting it requires a delicate therapeutic balance. Cardiologists reserve sodium channel blockers to treat potentially life-threatening ventricular tachycardia that does not respond to other treatment. The risks and complications of these medications are numerous and serious; they can cause fatal arrhythmias.

COMMON SODIUM CHANNEL BLOCKERS

disopyramide (Norpace)	flecainide (Tambocor)
mexiletine (Mexitil)	moricizine (Ethmozine)
procainamide (Pronestyl)	propafenone (Rythmol)
quinidine (Cardioquin, Quinidex)	

Thrombolytic Agents

Thrombolytic agents, commonly called "clot busters," dissolve blood clots that have already formed. Given early enough, they can prevent the

clot from forming, essentially halting heart attack or stroke before the event can cause any damage. However, doctors must administer them within three to four hours of clot formation. After four hours the clot has hardened and thrombolytic agents cannot dissolve them.

Thrombolytic agents are substances, either natural extracts or recombinant forms, that convert plasminogen in the blood to plasmin, an enzyme that dissolves fibrin. Fibrin is the substance in the blood that forms the webbing of the clot structure to snare platelets and other substances in the blood that become the clot. Early in the COAGULATION process fibrin is a semisolid, stringlike substance similar to the strands of a spiderweb. As the coagulation process continues, however, the fibrin strands and the cellular matter they have captured harden into the solid structure of a blood clot. Once the fibrin hardens, plasmin has no effect on it.

The most frequently used thrombolytic agents are tissue plasminogen activators (tPAs). One of the original thrombolytic agents, streptokinase, derives from the streptococcus bacterium and causes the body to develop antibodies against it. Because of this, doctors cannot administer streptokinase if the person has received streptokinase within 12 months. However, it takes about five days for the body to produce antibodies, allowing multiple administrations within five days of the initial dose. The tPAs do not seem to have this limitation, although it is possible for the body to develop antibodies against them as well.

Doctors administer thrombolytic agents intravenously to treat heart attack, stroke, deep vein thrombosis, and pulmonary embolism. The effect is rapid and short acting. Excessive and severe bleeding is a significant risk, particularly when stroke is hemorrhagic rather than ischemic. Doctors make every effort to determine the nature of a stroke before administering thrombolytic agents, though sometimes bleeding occurs even with ischemic stroke. As well, these agents may disturb the integrity of clots that have formed within the previous 10 days, such as from surgery.

COMMON THROMBOLYTIC AGENTS

alteplase (Activase)	anistreplase (Eminase)
reteplase (Retavase)	streptokinase (Streptase, Kabinase)
tenecteplase (TNKase)	urokinase (Abbokinase)

Vasoconstrictors

Vasoconstrictors cause the blood vessels to constrict, or tighten, to raise blood pressure. Doctors administer vasoconstrictors to treat cardiovascular SHOCK and HYPOTENSION. Many bronchodilating medications prescribed to treat asthma also have peripheral vasoconstriction action, and may raise blood pressure at the same time they open the airways. One of the most commonly used vasoconstrictors is pseudoephedrine, found in cold, flu, and some allergy medications. Caffeine and NICOTINE are also vasoconstrictors. Though doctors do not prescribe these products for cardiovascular use, they have the effect of raising blood pressure as well as increasing heart rate. The most commonly used vasoconstrictor for cardiovascular purposes is midodrine (ProAmatine).

Vasodilators

Many medications to treat hypertension are vasodilators, drugs that cause the blood vessels to relax so more blood can flow through them with less resistance. These medications may lower blood pressure or relieve angina pectoris. Among the general vasodilators cardiologists might prescribe to treat hypertension are hydralazine and minoxidil. Both drugs regulate the calcium that enters the smooth muscle cells of the ARTERY walls, slowing their contractility and causing the arteries to relax (dilate). Minoxidil is an NTI drug that requires close monitoring because, although it is a potent peripheral vasodilator, it also increases heart rate and has other cardiovascular actions that require additional medications to moderate.

Nitrate vasodilators are especially effective at relaxing the coronary arteries to relieve angina pectoris, which is one of the leading reasons doctors prescribe them. Nitrates also dilate the peripheral veins, which decreases the heart's workload. Nitrates come in sublingual tablets placed under the tongue at the onset of anginal symptoms, regular and long-acting oral medications, transdermal (skin) patches, and topical ointments. Because the body acquires a tolerance to nitrates, dosing schedules are particularly important. Other commonly prescribed medications that have vasodilating actions include certain of the beta blockers, calcium channel blockers, ACE inhibitors, and ARBs.

COMMON VASODILATORS

hydralazine (Apresoline)
mecamylamine (Inversine)
minoxidil (Loniten)

Nitrates

isosorbide dinitrate (Isordil, Sorbitrate)
isosorbide mononitrate (Imdur, ISMO, Monoket)
nitroglycerin (Nitro-Dur, Nitrolingual, Nitrostat)

See also ADRENAL GLANDS; ANTIBODY; BACTERIA; LIVING WITH CARDIOVASCULAR DISEASE.

microinfarction Tiny arterial occlusions that briefly block the flow of BLOOD to the BRAIN, causing transient ischemic attacks (TIAs), or to the HEART. What microinfarction lacks in initial effect it makes up through frequency. Microinfarction may also affect other key organs such as the KIDNEYS and LIVER. Conditions that can result in microinfarction include severe ATHEROSCLEROSIS, PERIPHERAL VASCULAR DISEASE (PVD), CORONARY ARTERY DISEASE (CAD), INTERMITTENT CLAUDICATION, and DEEP VEIN THROMBOSIS (DVT). Microinfarction also may

MEDICATIONS TO TREAT CARDIOVASCULAR CONDITIONS

Type of Medication	Common Products	Actions/Effects	Cardiovascular Conditions
ACE inhibitor	benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril	dilate peripheral arteries and arterioles; lower BLOOD PRESSURE	HEART FAILURE; HYPERTENSION; VALVULAR HEART DISEASE; used after HEART ATTACK to prevent subsequent heart attack
adenosine (intravenous hospital administration only)	adenosine	slow the HEART RATE	PAROXYSMAL ATRIAL TACHYCARDIA (PAT); WOLFF-PARKINSON-WHITE SYNDROME
alpha blocker	clonidine, doxazosin, guanabenz, guanfacine, labetalol, mecamylamine, methyldopa, phenoxybenzamine, prazosin, terazosin	block the actions of EPINEPHRINE and NOREPINEPHRINE on the HEART and arteries; dilate peripheral blood vessels; lower blood pressure	hypertension
angiotensin II receptor blocker	candesartan, eprosartan, irbesartan, losartan, telmisartan, valsartan	dilate peripheral arteries and arterioles; lower blood pressure	heart failure; hypertension
anticoagulant	dalteparin, enoxaparin, heparin, tinzaparin, warfarin	inhibit activation of CLOTTING FACTORS; reduce blood's ability to clot	ATRIAL FIBRILLATION; DEEP VEIN THROMBOSIS; heart attack prophylaxis; INTERMITTENT CLAUDICATION; STROKE prophylaxis; PERIPHERAL VASCULAR DISEASE; PULMONARY EMBOLISM
antiplatelet	aspirin, cilostazol, clopidogrel, dipyridamole, fondaparinux, ginkgo biloba, sulfinpyrazone, ticlopidine	inhibit PLATELET AGGREGATION; reduce blood's ability to clot	ANGINA PECTORIS; deep vein thrombosis; heart attack prophylaxis; intermittent claudication; stroke prophylaxis; STENT placement

Type of Medication	Common Products	Actions/Effects	Cardiovascular Conditions
beta blocker	acebutolol, atenolol, betaxolol, bisoprolol, carteolol, carvedilol, esmolol, labetalol, metoprolol, nadolol, penbutolol, pindolol, propranolol, sotalol, timolol	block the actions of epinephrine and norepinephrine on the heart and arteries; dilate the arteries; slow the heart rate; lower blood pressure	angina pectoris; atrial fibrillation; CARDIOMYOPATHY; heart failure; hypertension; PALPITATIONS; used after heart attack to prevent subsequent attack
calcium channel blocker	amlodipine, diltiazem, felodipine, isradipine, nicardipine, nifedipine, nimodipine, nisoldipine, verapamil	dilate arteries; relax myocardial cells; slow heart rate; lower blood pressure	angina pectoris; atrial fibrillation; cardiomyopathy; heart failure; hypertension
diuretic	amiloride, bumetanide, chlorthalidone, chlorothiazide, eplerenone, ethacrynic acid, furosemide, hydrochlorothiazide, indapamide, metolazone, polythiazide, spironolactone, torsemide, triamterene	reduce excess fluid; lower blood pressure; reduce heart's workload	edema; heart failure; hypertension
inotropic	digoxin, digitoxin	strengthen heart MUSCLE; slow heart rate in atrial fibrillation; reduce heart's workload	atrial arrhythmias; heart failure
lipid-lowering	atorvastatin, bezafibrate, cholestyramine, clofibrate, colesevelam, colestipol, ezetimibe, fenofibrate, fluvastatin, gemfibrozil, pitavastatin, lovastatin, rosuvastatin, simvastatin, niacin	limit lipid synthesis or absorption; lower cholesterol and triglyceride blood levels	HYPERLIPIDEMIA; statins after heart attack
nitrate	erythrityl tetranitrate, isosorbide dinitrate, isosorbide mononitrate, nitroglycerin, pentaerythritol tetranitrate	dilate arteries in the heart to increase blood flow to the heart; dilate veins in the body to decrease the heart's workload	angina pectoris
potassium channel blocker	amiodarone, dofetilide, ibutilide	regulate heart rate	atrial fibrillation; atrial tachycardia

Type of Medication	Common Products	Actions/Effects	Cardiovascular Conditions
sodium channel blocker	disopyramide, flecainide, mexiletine, moricizine, procainamide, propafenone, quinidine, tocainide	slow electrical conduction in the heart; regulate heart rate	severe ventricular tachycardia
thrombolytic (intravenous hospital administration only)	anistreplase, streptokinase, tissue plasminogen activator (tPA), urokinase	dissolve blood clots	deep vein thrombosis; ischemic stroke; MYOCARDIAL INFARCTION
vasoconstrictor	epinephrine	constrict blood vessels; raise blood pressure	HYPOTENSION
vasodilator	hydralazine, isosorbide dinitrate, isosorbide mononitrate, mecamylamine, minoxidil, nitroglycerin	dilate blood vessels; decrease the heart's workload; lower blood pressure	angina pectoris; CORONARY ARTERY DISEASE; hypertension

occur after surgical operations or major trauma, when clot fragments break away from HEALING wounds. Doctors use ANTICOAGULATION THERAPY to control microinfarction.

See also ASPIRIN THERAPY; HEART ATTACK; ISCHEMIC HEART DISEASE; KIDNEY; MYOCARDIAL INFARCTION; STROKE; TRANSIENT ISCHEMIC ATTACK (TIA).

minimally invasive cardiac surgery Surgical methods that combine ENDOSCOPY and CARDIAC CATHETERIZATION to repair damaged HEART valves or clear obstructive ATHEROSCLEROTIC PLAQUE. Some methods involve making several small incisions in the chest and between the ribs to gain access to the heart. Others involve inserting microscopic tools, via cardiac catheterization, into the heart. There remain questions as to whether minimally invasive cardiac surgery is of greater or lesser risk than OPEN HEART SURGERY.

Though significantly less traumatic, minimally invasive cardiac surgery restricts the surgeon's ability to see the condition of the heart. Minimally invasive cardiac surgery done "off-pump" (without CARDIOPULMONARY BYPASS), further challenges the surgeon's ability to operate on a moving target. Countering these concerns are the reduced trauma to the chest because the STERNUM (breastbone) can remain intact, as well as avoiding the risks of cardiopulmonary bypass. Recovery is much more rapid and significantly less painful than with traditional open heart surgery. However, the surgeon cannot reach the back of the heart using minimally invasive procedures, limiting the value of these methods for treating CORONARY ARTERY DISEASE (CAD) that involves the posterior CORONARY ARTERIES.

See also MINIMALLY INVASIVE SURGERY; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

myocardial infarction Death of HEART tissue. The most common cause of myocardial infarction is occlusion of the CORONARY ARTERIES such as occurs as a consequence of CORONARY ARTERY DISEASE (CAD) or less frequently of coronary ARTERY spasm. Myocardial infarction is the clinical term doctors use for HEART ATTACK. The MYOCARDIUM has very high oxygen needs, as oxygen is the only energy source for myocardial cells (unlike most other cells in the body, except the BRAIN, that also use GLUCOSE for energy). Myocardial tissue does not have significant ability to regenerate.

Myocardial tissue that dies not only can no longer contract to aid in the heart's function but

also cannot conduct electrical impulses to reach undamaged tissue. Myocardial infarction results in "dead" areas of the heart MUSCLE that cannot participate in the CARDIAC CYCLE, which often results in ARRHYTHMIA as well as ineffective pumping ability. The cellular structure of these areas changes, initially becoming soft and subsequently becoming fibrous (scarlike). New arteries are often able to develop, through a process called angiogenesis, to carry BLOOD around infarcted areas of the heart. This helps the rest of the heart remain functional. However, large infarctions may overcome the heart, resulting in heart attack or CARDIAC ARREST.

ELECTROCARDIOGRAM (ECG) and ECHOCARDIOGRAM are the diagnostic procedures that typically identify myocardial infarction. Treatment includes eliminating the cause of the infarction, such as coronary artery occlusion, and stabilizing the heart's function to the best extent possible with medications. Because CAD is nearly always the culprit, ANGIOPLASTY or CORONARY ARTERY BYPASS GRAFT (CABG) are nearly always among the treatment options.

See also CARDIOVASCULAR DISEASE PREVENTION; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; MICROINFARCTION; MYOCARDIAL PERFUSION IMAGING; STROKE; SURGERY BENEFIT AND RISK ASSESSMENT; TRANSIENT ISCHEMIC ATTACK (TIA).

myocardial perfusion imaging A radionuclide procedure that allows cardiologists to observe the flow of BLOOD from the CORONARY ARTERIES into the tissues of the MYOCARDIUM (HEART MUSCLE). The test usually involves a resting and an exercise component, to provide a comprehensive picture of how much blood the heart receives to assess the extent to which CORONARY ARTERY DISEASE (CAD) is reducing cardiac function. The procedure takes about an hour and requires little preparation (namely, abstaining from STIMULANTS such as CAFFEINE and NICOTINE for 48 hours before the procedure).

The cardiologist administers a small amount of a radioactive substance, called a radionuclide or radioisotope (most commonly thallium), into a VEIN in the back of the hand or in the arm. The radionuclide is mixed in a solution, usually GLUCOSE, that the blood carries to the cells. The radionuclide rides along as a "tag" on the glucose molecules, accompanying them into the cells. The radionuclide rapidly disintegrates, releasing a pattern of electromagnetic energy called gamma-rays. A special device called a gamma camera detects the gamma rays, and presents them as images. The concentrations of energy tell cardiologists where myocardial blood flow is strong and where it is restricted, helping identify areas of ischemia (oxygen-deprived tissue).

When actual physical exercise is not feasible, the cardiologist may use a DRUG (often dipyridamole) to chemically simulate the effects of exercise on the heart. People who have ANGINA PECTORIS or significant CAD may feel temporary discomfort during this simulation. There are no side effects from myocardial perfusion imaging. The radionuclides cardiologists use emit minimal radioactivity and are gone from the body within a few hours.

See also COMPUTED TOMOGRAPHY (CT) SCAN; ECHOCARDIOGRAM; MAGNETIC RESONANCE IMAGING (MRI); POSITRON EMISSION TOMOGRAPHY (PET) SCAN; SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT) SCAN.

myocarditis INFLAMMATION of the HEART MUSCLE, often as a consequence of viral INFECTION that originates elsewhere in the body (such as a cold). Viruses known to cause myocarditis include MEASLES, RUBELLA, coxsackie, and CYTOMEGALOVIRUS (CMV). Myocarditis also may be bacterial, or the consequence of cardiotoxic exposure (such as to radiation or carbon monoxide). The autoimmune processes of systemic inflammatory disorders such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), SARCOIDOSIS, and RHEUMATOID ARTHRITIS also can involve the myocardium. A rare and severe form of myocarditis is giant cell myocarditis, an autoimmune disorder that specifically attacks the heart.

Myocarditis may have few symptoms until there is significant damage to the heart (commonly in the form of CARDIOMYOPATHY and ARRHYTHMIA), and often is life-threatening. Symptoms of early or chronic myocarditis may mimic those of INFLUENZA or of HEART ATTACK. Diagnosis is by myocardial biopsy performed via CARDIAC CATHETERIZATION, which reveals the infiltration of lymphatic cells and other characteristic changes in the myocardium that identify an inflammatory process. Chronic or advanced myocarditis may

have FIBROSIS (scar tissue). Treatment targets relieving arrhythmias and HEART FAILURE, and may include IMMUNOSUPPRESSIVE THERAPY. HEART TRANSPLANTATION may become an option for end-stage heart failure.

See also AUTOIMMUNE DISORDERS; BACTERIA; COLDS; ENDOCARDITIS; PERICARDITIS; VIRUS.

myocardium The MUSCLE tissue that forms the walls of the HEART. Myocardial cells are unique in their structure, blending muscle and NERVE structures so they can both contract and conduct electrical impulses. Myocardial cells thus can contract independent of external stimulation. The myocardial fibers of the atria have a different configuration from those of the ventricles. The CORONARY ARTERIES provide an extensive network to supply blood to the myocardium, which requires about 70 percent of the blood's oxygen. With increasing age, fibrous and fatty tissue tends to infiltrate the myocardium, somewhat reducing its effectiveness.

CONDITIONS THAT CAN AFFECT THE MYOCARDIUM

CARDIOMYOPATHY	CONGENITAL ANOMALY
ISCHEMIC HEART DISEASE	MICROINFARCTION
MYOCARDIAL INFARCTION	MYOCARDITIS

CORONARY ARTERY DISEASE (CAD) is the most significant threat to the myocardium, as occlusions in the coronary arteries deprive the myocardium of blood and thus oxygen. When the consequence is MYOCARDIAL INFARCTION, CARDIAC ARREST can result.

For further discussion of the myocardium within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also ENDOCARDIUM; HEART FAILURE; PERICARDIUM.

myxoma A nonmalignant tumor that grows in the HEART, nearly always in one of the atria and most commonly in the left atrium. Myxoma arises from the ENDOCARDIUM and may be either firm or soft in consistency. The tumor can block the flow of BLOOD through the atrium, interfere with the function of the heart valves, or break apart to send fragments into the blood circulation that cause embolism (sudden blockage of an ARTERY) elsewhere in the body. Soft myxomas are more likely to fragment; firm myxomas are more likely to be occlusive. As a myxoma grows it causes increasing turbulence in the blood as it flows through the chamber, presenting a significant risk for the formation of blood clots. ECHOCARDIOGRAM generally provides definitive diagnosis. Treatment is OPEN HEART SURGERY to remove the tumor. Once removed, the tumor results in no residual consequences. Myxoma is most common in people between the ages of 30 years and 60 years.

See also ATRIAL FIBRILLATION; TRANSIENT ISCHEMIC ATTACK.

obesity and cardiovascular disease OBESITY, a condition in which excess body weight is 20 percent or more above healthy weight as a result of excessive body fat, emerged in the 1990s as an independent risk factor for CARDIOVASCULAR DISEASE (CVD). This means that without any other additional RISK FACTORS FOR CARDIOVASCULAR DISEASE, obesity makes CVD more likely. However, the relationship between obesity and CVD is complex. Other health conditions associated with obesity also increase the risk for numerous types of cardiovascular disease. Prominent among them are HYPERTENSION (high BLOOD PRESSURE), INSULIN RESISTANCE, HYPERLIPIDEMIA, and DIABETES. Some health experts believe obesity is as significant a risk factor for cardiovascular disease as cigarette smoking.

Doctors define obesity as a BODY MASS INDEX (BMI) of 30 kilograms per meter squared (kg/m^2) or higher. This corresponds to about 20 percent above healthy weight. BMI correlates body weight with health risk. At a BMI of 30, a person is likely to have at least one health condition associated with obesity. As BMI rises, so do the associated health conditions and the risk for cardiovascular disease. When BMI reaches 40, it is unusual for there *not* to be some form of cardiovascular disease present.

Obesity affects cardiovascular function mechanically and metabolically. Excessive body fat pressures the BLOOD vessels, causing the heart to work harder to pump blood through them. As well, there is more surface area that the cardiovascular

BMI AND CARDIOVASCULAR DISEASE RISK

BMI (kg/m2)	Cardiovascular Risk	Conditions
18.5–24.9: healthy	not affected	none
25–29.9: overweight	increased	HYPERLIPIDEMIA; HYPERTENSION manageable through lifestyle
30–34.9: OBESITY	high	hyperlipidemia; hypertension; ATHEROSCLEROSIS manageable through lifestyle and medication
35–39.9: severe obesity	very high	hyperlipidemia; hypertension; atherosclerosis; mild to moderate CORONARY ARTERY DISEASE (CAD); DIABETES (type 2); OBSTRUCTIVE sleep apnea management requires multiple medications
40+: morbid obesity	extremely high	hyperlipidemia; hypertension; atherosclerosis; moderate to severe CAD; symptomatic HEART FAILURE; diabetes; obstructive sleep apnea multiple medications necessary though may not entirely manage cardiovascular conditions

system must perfuse with blood. Excessive body fat may compress the neck, causing OBSTRUCTIVE SLEEP APNEA (episodes during sleep in which the person stops BREATHING). Obstructive sleep apnea prevents adequate air flow to the LUNGS, reducing oxygenation of the blood and causing ischemic episodes in which the heart does not receive enough oxygen, which results in ARRHYTHMIA. Excessive body fat may also compress the heart itself, further increasing the forces against which it must work to pump blood. All of these factors conspire to raise blood pressure and increase HEART RATE in an attempt to help the heart, which, if allowed to progress unchecked, are likely to result in HEART FAILURE.

Metabolically, obesity triggers INSULIN dysfunction. Because insulin plays a key role in cholesterol synthesis in the LIVER, hyperlipidemia is likely. Hyperlipidemia contributes to CORONARY ARTERY DISEASE (CAD) and PERIPHERAL VASCULAR DISEASE (PVD). A more significant health concern is the evolution from insulin resistance to diabetes. Diabetes increases cardiovascular disease risk substantially, as it is itself an independent risk factor for, as well as a leading cause of, cardiovascular disease.

When obesity declines even modestly, cardiovascular risk drops and cardiovascular health improves. As little as a 10-pound weight loss can drop systolic blood pressure by 10 millimeters of mercury (mm Hg). With sustained weight loss, many cardiovascular symptoms retreat and risk continues to fall.

See also BODY FAT PERCENTAGE; CARDIOVASCULAR DISEASE PREVENTION; EATING HABITS; DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND CARDIOVASCULAR HEALTH; OBESITY AND DIABETES; WEIGHT LOSS AND WEIGHT MANAGEMENT.

omega fatty acids and cardiovascular health Omega fatty acids are dietary substances that increase high-density lipoprotein cholesterol (HDL-C) and decrease low-density lipoprotein cholesterol (LDL-C). Omega fatty acids also reduce the likelihood of ARRHYTHMIA and may help lower BLOOD PRESSURE. The omega fatty acids that appear most beneficial are eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Researchers do not know how omega fatty acids affect cardiovascular health though believe they reduce INFLAMMATION and the blood's clotting tendencies. These effects slow ATHEROSCLEROTIC PLAQUE accumulation and infiltration into the arterial intima, the innermost layer of the arterial wall.

The most abundant dietary sources of omega fatty acids are cold-water fish such as mackerel, tuna, and salmon. Health experts recommend eating at least two servings a week of these fish, which contain high levels of EPA and DHA, or taking supplements that provide 1 to 1.5 grams of EPA and DHA. People who have high levels of triglycerides may need to take higher doses. However, doses higher than 3 grams may cause excessive bleeding. Flaxseed and flaxseed oil, canola oil, soybeans and soybean foods such as tofu, and walnuts are good dietary sources of alpha-linolenic acid (LNA), from which the body can metabolize omega fatty acids.

An unresolved concern remains that of mercury contamination in cold-water fish. Mercury poisoning is particularly harmful to a developing FETUS and raises the risk for certain kinds of CANCER in adults. The US Environmental Protection Agency (EPA) routinely samples and reports mercury levels in different species of fish and issues advisories for those that exceed established safety levels. People who are concerned about mercury contamination can obtain omega fatty acids through dietary supplements, which appear equally effective.

See also CARDIOVASCULAR DISEASE PREVENTION; DIET AND CARDIOVASCULAR HEALTH; DIET AND HEALTH; NUTRITIONAL NEEDS; NUTRITIONAL SUPPLEMENTS.

open heart surgery Any OPERATION in which the surgeon opens the chest to expose the HEART. Open heart surgery is the most common method for CORONARY ARTERY BYPASS GRAFT (CABG), valvuloplasty and heart valve replacement, reconstructive operations to correct congenital heart malformations, and HEART TRANSPLANTATION. In the United States, surgeons perform about 750,000 open heart surgery operations each year, about 600,000 of which are CABG. Open heart surgery requires general ANESTHESIA and a hospital stay of 3 to 10 days, depending on the operation. Though most open heart operations also employ CARDIOPULMONARY BYPASS, in which a machine takes over the role of oxygenating and pumping the BLOOD so the

surgeon can operate on a still heart, there is a growing trend toward "off pump" operations that do not use cardiopulmonary bypass.

Surgical Procedure

For open heart surgery, the surgeon makes a long incision lengthwise along the top of the sternum (breastbone) through the SKIN and tissues beneath, and then makes a similar saw-cut through the sternum to enter the chest cavity. Special retractors spread the sternum and hold the incision open. To reach the heart, the surgeon must open the PERICARDIUM, the protective membranous sac that surrounds the heart. Often the surgeon leaves the pericardium open after the operation on the heart, to shorten surgery time and reduce the risk for postoperative complications.

For operations using cardiopulmonary bypass, the surgeon attaches the heart's major vessels to large tubes called cannulas, then clamps the heart vessels closed. The blood reroutes through the bypass machine. The surgeon can then bathe the heart in a cold concentrated potassium solution, which causes the heart to stop beating (cardioplegia). After completing the operation the surgeon reverses the process to restore circulation through the heart, closes the sternum with sturdy wire sutures and the skin with nylon sutures or staples. The SCAR that remains after the surgical wound heals remains fairly prominent for two to three years, after which it fades to a thin line.

When the operation is "off pump," the surgical team lowers the person's body temperature to slow body functions including heart contractions. The surgeon operates on the moving heart, which requires precise technique and timing. Inadvertent damage to the heart is a significant risk.

Risks and Complications

Many of the risks of open heart surgery are the same regardless of the operation. Key among them are

- excessive bleeding due to anticoagulants
- air embolism during cardiopulmonary bypass, which can cause STROKE
- difficulty restoring the heart to normal rhythm
- failure of the surgical procedure
- surgeon error
- unexpected anatomic anomalies

General complications that can occur after surgery include

- bleeding at the operative site or at the surface surgical wound
- INFECTION, either affecting the heart or the surgical wound
- blood clots, which may cause PULMONARY EMBOLISM, HEART ATTACK, or stroke
- ARRHYTHMIA
- HYPERTENSION and HEART FAILURE

Surgeons and the health-care team are alert for complications that can arise. Most people stay for 12 to 48 hours in a specialized cardiac surgery intensive care unit, where staff monitor cardiopulmonary function continuously. Many potential postoperative complications become less likely by 48 hours from surgery, though many people stay in the hospital for up to 10 days until the surgeon is confident that HEALING is well under way.

Outlook and Lifestyle Modifications

The outlook following open heart surgery depends to great extent on the reason the surgery was necessary. Many people return to normal activities after they recover from their operations, though may require frequent follow-up visits or medications. This is especially true for heart transplant recipients. The likelihood of complications diminishes as time passes and healing becomes complete.

Most people need to make some lifestyle changes after open heart surgery, typically in eating and exercise habits. Cardiologists recommend a diet that is nutritiously balanced and daily exercise such as walking. CARDIAC REHABILITATION programs help people get started with such changes, providing customized plans to accommodate the person's starting point as well as recovery goals.

See also LIFESTYLE AND CARDIOVASCULAR HEALTH; LIVING WITH CARDIOVASCULAR DISEASE; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

Ornish program An intensive lifestyle-oriented method for reducing the risk for CORONARY ARTERY

DISEASE (CAD) and HEART ATTACK. Named for Dean Ornish, the American physician who developed the approach, the Ornish program features a strict vegetarian diet very low in fat along with daily YOGA, walking, MEDITATION, and participation in SUPPORT GROUPS. In the early 2000s in the United States, Medicare approved the Ornish program as an alternative treatment approach for CAD and rehabilitation following heart attack. The program arises from 25 years of clinical research supporting the effectiveness of restrictive diet to halt and sometimes reverse CAD. Numerous cardiovascular rehabilitation centers around the country offer the Ornish program. It is important to maintain the lifestyle changes after completing the structured program.

See also CARDIOVASCULAR DISEASE PREVENTION; LIFESTYLE AND CARDIOVASCULAR HEALTH.

P

pacemaker A small, implanted electronic device that emits electrical impulses to maintain a regular HEART RATE. The most frequent use of a pacemaker is to treat bradycardia, an ARRHYTHMIA in which the HEART rate is persistently below 60 beats per minute. A pacemaker may also be an effective treatment for obstructive CARDIOMYOPATHY, in which thickening of the heart wall interferes with the ability of the myocardial cells to convey electrical impulses.

Implanting the Pacemaker

The cardiologist implants the pacemaker during a brief procedure, with local anesthetic and a mild sedative to make the person comfortable. A standard pacemaker has two components: the pacing lead and the computerized control unit. The pacing lead extends through a BLOOD vessel into the heart, where the cardiologist positions it against the wall of the heart, usually the right ventricle or the right atrium. Some pacemakers may have two pacing leads, with one going into the right atrium and the other to the right ventricle.

The cardiologist then makes a small incision just below the collarbone to create a pocket that holds the control unit, and connects the pacing lead to the control unit. The cardiologist then programs the control unit to deliver an electrical impulse, a very mild electrical shock, when the heart rate falls below a specific threshold. Most pacemakers are set to respond "on demand," which means they emit pacing impulses only when the heart fails to generate them itself. The incision over the pacemaker control unit heals in about two or three weeks, leaving a barely noticeable protrusion.

Living with a Pacemaker

Some people notice when the pacemaker releases an electrical impulse, though most people are not aware. The "on demand" feature of current pacemakers allows the heart to accelerate its rhythm during physical exercise, sexual activity, and other situations in which the heart would naturally beat faster. Certain medical and dental equipment, such as MAGNETIC RESONANCE IMAGING (MRI), machines that deliver RADIATION THERAPY, and some dental drills also can interfere with pacemakers. Though earlier models of pacemakers were sensitive to electromagnetic interference from household appliances and other electronic devices, this is no longer the case. Only high-power devices such as welding equipment or power tools emit enough electromagnetic energy to disrupt a pacemaker. There is some question about the potential of interference from cellular and portable telephones. To be safe, cardiologists recommend keeping the phone at least six inches from, and holding it to the ear opposite, the pacemaker's control unit. Pacemakers run on lithium batteries and can function for about seven years before they need to be replaced.

See also CARDIAC RESYNCHRONIZATION THERAPY (CRT); IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD); MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; RADIOFREQUENCY ABLATION.

palpitations Perception that the HEART is racing, pounding, or skipping beats. Palpitations are may represent signs of underlying cardiovascular conditions such as ARRHYTHMIA though frequently signal high stress, anxiety, or excessive consumption of STIMULANTS such as CAFFEINE or NICOTINE (via cigarette smoking). When palpitations do suggest arrhythmia, they tend to occur along with other symptoms such as weakness and SYNCOPE (fainting). Awareness of the heartbeat is common during or immediately following strenuous exercise,

when the heart feels as if it were pounding, and right before falling asleep at night.

SUBSTANCES THAT CAN CAUSE PALPITATIONS	
albuterol	ALCOHOL
CAFFEINE	COCAINE
levothyroxine	ma huang
NICOTINE (tobacco)	pseudoephedrine
theophylline	

The most common presentation of palpitations is the premature beat, which can be atrial or ventricular and feels like a skipped beat though it is not. Because the premature beat is early, there is a slight pause before the regular beat which makes the regular beat feel enhanced. Such palpitations are nearly always the result of stimulants (including cold and flu preparations) or anxiety, and go away either when the stopping the stimulant or removing the cause of stress.

Palpitations require a doctor's evaluation when they occur

- frequently or for sustained periods of time
- with syncope or lightheadedness
- with chest discomfort
- with shortness of breath (DYSPNEA)
- in people who have diagnosed forms of CARDIOVASCULAR DISEASE (CVD) such as HYPERTENSION, CORONARY ARTERY DISEASE (CAD), and arrhythmia disorders

The arrhythmia disorders most likely to include palpitations among their symptoms are ATRIAL FIBRILLATION and PAROXYSMAL ATRIAL TACHYCARDIA (PAT), also called paroxysmal supraventricular tachycardia (PSVT). These disorders typically cause periods of rapid heartbeat. Though disconcerting, these arrhythmias are rarely dangerous. HYPERTHYROIDISM may also cause palpitations, which go away with treatment for the hyperthyroidism.

An ELECTROCARDIOGRAM (ECG) provides the necessary information to determine whether palpitations indicate an arrhythmia or other heart problem. A Holter monitor (24-hour recording of the heart's electrical activity) and an exercise STRESS TEST help identify arrhythmias and conduction disorders that are intermittent or brought on by physical exertion. Unless there is a significant underlying arrhythmia disorder, there is no need to treat palpitations. MEDITATION, relaxation techniques, and eliminating substances that can have a stimulant effect on the heart often reduce or end the palpitations.

See also PREMATURE VENTRICULAR CONTRACTION (PVC); LONG QT SYNDROME (LQTS); WOLFF-PARKINSON-WHITE SYNDROME.

paroxysmal atrial tachycardia (PAT) An ARRHYTHMIA disorder, also called paroxysmal supraventricular tachycardia (PSVT), in which the atria have episodes of rapid, regular contractions. "Paroxysmal" means the symptoms start and stop abruptly, without apparent cause. During a PAT episode, the HEART RATE may reach 140 beats per minute. The atrial contractions of PAT originate in the atrium above the ATRIOVENTRICULAR (AV) NODE rather than in the SINOATRIAL (SA) NODE that usually initiates the heart's electrical pacing impulses.

The normal path for pacing impulses is from the SA node through the atria to the AV node. Many people who have PAT have more than one conduction pathway at the AV node. Errant electrical impulses from myocardial cells in the atrium can activate the alternate pathway, called an accessory pathway, triggering atrial contractions. These are called reentrant atrial tachycardias; PAT is one variation. An episode of PAT may last a few minutes or several days. The longer the episode lasts, the more likely it is to produce symptoms.

The primary symptoms of PAT are PALPITATIONS and lightheadedness, dizziness, or SYNCOPE (fainting). Some people experience CHEST PAIN, fatigue, and shortness of breath during an episode of PAT, though feel fine otherwise. Diagnosis is by ELECTROCARDIOGRAM (ECG), which may require Holter monitor to capture episodes as they occur. Treatment may include medications that can disrupt the accessory AV pathway, such as adenosine or calcium channel blockers. RADIOFREQUENCY ABLATION, which destroys a small portion of the conductive pathway to prevent electrical impulses from traveling it, is often a viable treatment option for people with recurrent PAT and usually puts a permanent end to the episodes.

See also ATRIAL FIBRILLATION; HEART; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE.

percutaneous transluminal coronary angioplasty (PCTA) See ANGIOPLASTY.

pericarditis INFLAMMATION of the PERICARDIUM, the membranous sac that surrounds and protects the HEART. Pericarditis can be acute (comes on suddenly) or chronic (intermittent symptoms over a period of time), the result of an INFECTION or an autoimmune disorder such as RHEUMATOID ARTHRITIS. Infections are usually viral, with the coxsackie VIRUS and echovirus the most common culprits, though viral pericarditis may follow INFLUENZA or accompany AIDS. Bacterial pericarditis is less common and may occur after bacterial infection elsewhere in the body (such as STREP THROAT) or as a complication of an OPEN HEART SURGERY. Pericarditis may also develop after HEART ATTACK as an inflammatory response, typically with symptoms that begin within five days of the heart attack. Chronic pericarditis generally results from inflammatory processes not related to infection. Certain cancers, notably LEUKEMIA and KAPOSI'S SARCOMA, can involve the pericardium, causing ongoing or intermittent symptoms.

Any CHEST PAIN that persists longer than five minutes, especially pain that radiates into the arm and back, requires emergency medical evaluation to rule out HEART ATTACK.

The primary symptoms of pericarditis are PAIN from the chest, usually that radiates to the back or into the upper arm and shoulder, COUGH, and shortness of breath. Pain is usually sharp, worse with BREATHING in or lying down and relieved when sitting or standing upright. These symptoms are initially difficult to distinguish from heart attack, and typically result in emergency medical evaluation to determine whether heart attack is taking place. Many people have FEVER with acute pericarditis, and upon AUSCULTATION (listening to the chest with a STETHOSCOPE) the doctor can hear a characteristic sound called a friction rub. The pain of pericarditis comes from the pericardium, not the heart, a result of the pericardium rubbing against the heart or the LUNGS and chest cavity.

A potentially life-threatening complication of pericarditis is the rapid accumulation of fluid in the pericardial space, a filmy envelope in the pericardium's inner layer that normally contains a small amount of fluid to lubricate the beating heart. The fibrous outer pericardium does not have much ability to stretch to accommodate increased fluid, so the fluid instead pushes inward against the heart. The pressure restricts the heart's ability to contract to fill with BLOOD, resulting in a dangerous condition called cardiac tamponade. BLOOD PRESSURE and HEART RATE drop perilously in cardiac tamponade, and the compression can cause the heart to stop beating entirely. Some increase in fluid usually occurs with pericarditis, as that is part of the body's protective response to inflammation. When gradual and limited, such fluid increase does not usually affect the heart's function as the pericardium can slowly expand in response.

The diagnostic path includes ELECTROCARDIOGRAM (ECG), which reveals any arrhythmias or strain on the heart, and ECHOCARDIOGRAM to visualize the heart and its related structures. Echocardiogram usually shows the inflammation and any fluid accumulation, and helps distinguish pericarditis from other conditions such as heart attack or restrictive HEART FAILURE. Additional imaging procedures may include COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI). Treatment may include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve inflammation and pain, or CORTICOSTEROID MEDICATIONS if the inflammation is severe. Pericardiocentesis, in which the doctor uses a long needle and syringe to withdraw fluid from the pericardium, is necessary when fluid accumulation pressures the heart. Pericardiocentesis can determine whether the pericarditis is bacterial, in which case the doctor administers ANTIBIOTIC MEDICATIONS as well.

Most people who do not have underlying CARDIOVASCULAR DISEASE (CVD) or other significant systemic conditions make full and complete recovery within two or three weeks. Pericarditis can complicate cardiovascular disease. Systemic AUTOIMMUNE DISORDERS or inflammatory conditions may result in chronic pericarditis that may require ongoing anti-inflammatory therapy, usually with NSAIDs.

See also BACTERIA; CARDIOVASCULAR DISEASE PREVENTION; CORONARY ARTERY BYPASS GRAFT (CABG);

ENDOCARDITIS; HIV/AIDS; MYOCARDITIS; TAMPONADE, CARDIAC.

pericardium A tough, two-layer membranous sac that encloses the HEART. The pericardium's fibrous outer layer, called the fibrous pericardium, protects the heart from contact with the chest wall and other structures in the chest, including the LUNGS and the sternum. The pericardium wraps completely around the heart, extending around the bases of the great vessels (AORTA, superior and inferior VENA CAVA, pulmonary ARTERY, pulmonary VEIN) as they arise from the heart. Two ligaments attach the top of the pericardium to the back of the sternum. Other ligaments loosely connect the bottom of the pericardium to the DIAPHRAGM. These structures anchor the heart in its place in the chest.

The inner layer of the pericardium is a filmy envelope. Its two surfaces are the parietal pericardium, which contacts the fibrous pericardium, and the epicardium, which covers the MYOCARDIUM somewhat like a wet tissue. Inside the envelope is a watery fluid that lubricates the heart. The inner pericardium forms a nearly frictionless containment field for the beating heart. The pericardium is vulnerable to INFLAMMATION and INFECTION (PERICARDITIS).

For further discussion of the pericardium within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also ENDOCARDIUM; LIGAMENT.

peripheral vascular disease (PVD) ATHEROSCLEROSIS that affects the peripheral arteries, notably those in the legs. ATHEROSCLEROTIC PLAQUE infiltrates the inner wall of the arteries, the intima. This causes the intima to thicken and stiffen, restricting the FLEXIBILITY of the ARTERY as well as narrowing the passage for BLOOD (arterial lumen). PVD can affect the largest to the smallest of the peripheral arteries and is the cause of INTERMITTENT CLAUDICATION as well as often an underlying factor in ERECTILE DYSFUNCTION. NEUROPATHY of DIABETES can severely exacerbate PVD, resulting in restricted circulation and limb ischemia (oxygen deprivation) that can cause tissue death (GANGRENE). PVD due to diabetes is a leading cause of limb amputation. PVD also may contribute to HYPERTENSION (high BLOOD PRESSURE).

Symptoms and Diagnostic Path

PVD often has firmly established itself by the time symptoms manifest. Intermittent claudication—PAIN with walking—is the primary symptom of PVD affecting the lower extremities. Leg or foot pain at rest, with coolness and pallor or CYANOSIS of the limb, suggests embolism (clot or atherosclerotic fragment blocking the flow of blood). Other symptoms may include lack of sensation (PARESTHESIA) or inability to move the limb (PARALYSIS), and wounds that do not heal. In severe PVD there is sometimes a mottled appearance to the SKIN. The doctor may be unable to feel a PULSE in the leg or foot, depending on the level of the occlusion or embolism. The diagnostic path often includes Doppler ULTRASOUND examination, and sometimes MAGNETIC RESONANCE IMAGING (MRI), of the legs.

Treatment Options and Outlook

The primary thrust of treatment when symptoms are present is ANTICOAGULATION THERAPY, which may include intravenous heparin when the doctor suspects an embolism. For symptoms such as intermittent claudication or rest ischemia, the treatment is typically the oral anticoagulant warfarin or antiplatelet agents such as cilostazol to reduce the risk for clot formation. A program of progressive walking improves blood flow in the legs as well as strengthens the leg muscles so they can provide additional support for the blood vessels. Weight loss reduces pressure on the arteries. The treatment regimen often includes lipid-lowering medications in conjunction with lifestyle modifications to lower blood lipid levels, which are usually elevated in PVD. Lifestyle changes include daily physical exercise such as walking, nutritious EATING HABITS, and SMOKING CESSATION. When symptoms fail to improve with these therapeutic measures, the doctor may consider ATHERECTOMY, an OPERATION to remove segments of atherosclerotic plaque from the arterial walls. Many people who have intermittent claudication benefit from wearing support stockings, which are tight against the legs to help support the blood vessels.

PVD is a progressive condition closely linked with CORONARY ARTERY DISEASE (CAD). Therapeutic

approaches, which must include lifestyle modifications to be successful, often can slow its progress.

Risk Factors and Preventive Measures

The risk factors for PVD include smoking, other atherosclerotic disease processes such as CAD, diabetes, and HYPERLIPIDEMIA. Controlling or eliminating these factors reduces the risk for PVD. Once PVD shows symptoms, then the most effective approach is aggressive management to prevent the condition from worsening.

See also ATRIAL FIBRILLATION; CARDIOVASCULAR DISEASE PREVENTION; DEEP VEIN THROMBOSIS (DVT); WALKING FOR FITNESS.

physical exercise and cardiovascular health The influence of regular physical activity on the structures and functions of the cardiovascular system. Regular AEROBIC EXERCISE has numerous effects on the cardiovascular system, improving the heart's pumping efficiency as well as the circulation's oxygen transport to the tissues of the body. It also improves the efficiency with which cells throughout the body, and notably those of skeletal MUSCLE, use oxygen. This decreases demand on the HEART, generally slowing the HEART RATE and decreasing BLOOD PRESSURE. As well, physical activity increases INSULIN sensitivity, which helps the body maintain a healthy BLOOD lipid balance to reduce the risk for HYPERLIPIDEMIA.

PHYSICAL EXERCISE RECOMMENDATIONS

- 30 to 45 minutes of moderate physical activity five to seven days a week
- 20 to 45 minutes of vigorous physical exercise three to four days a week

Health experts consider physical inactivity to be the prime lifestyle factor contributing to most acquired CARDIOVASCULAR DISEASE (CVD). Though recommendations call for 30 minutes of moderate physical exercise daily and 30 to 45 minutes of vigorous aerobic exercise three to four times a week, fewer than 20 percent of American adults are physically active at these levels and about 20 percent get no physical exercise at all. Health experts attribute at least 250,000 of deaths from cardiovascular disease to physical inactivity. Yet the level of physical activity that could prevent these deaths is minimal, only 30 minutes a day of moderately brisk walking (a pace of 3 to 4 miles per hour).

Small amounts of moderately intense physical activity that accumulate to the recommended exercise times are equally effective as contiguous blocks of exercise time, an important finding to emerge from recent research into the relationship between physical activity and cardiovascular health. Meeting the recommended minimum activity levels could prevent as much as 40 percent of cardiovascular disease. Ideal activities for cardiovascular health include walking, bicycling, running, and swimming.

See also AEROBIC FITNESS; CARDIOVASCULAR DISEASE PREVENTION; DIET AND CARDIOVASCULAR HEALTH; DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND CARDIOVASCULAR HEALTH; WALKING FOR FITNESS.

premature ventricular contraction (PVC) An early heartbeat that causes the sensation of a skipped beat. Most often PVCs are harmless. They may occur spontaneously, without apparent cause, and are most noticeable at rest or following strenuous exercise. CAFFEINE, pseudoephedrine (a vasoconstrictor and stimulant common in cold and allergy products), NICOTINE (tobacco), and anxiety (stress) may also cause PVCs. PVCs require a doctor's evaluation when they occur

- frequently
- repeatedly over a period of time rather than in isolation
- with CHEST PAIN or discomfort
- with lightheadedness, dizziness, or SYNCOPE (fainting)

A doctor also should evaluate PVCs in anyone who has diagnosed CARDIOVASCULAR DISEASE (CVD), particularly an ARRHYTHMIA disorder. Occasionally PVCs can trigger a more serious arrhythmia such as ventricular tachycardia. An ELECTROCARDIOGRAM (ECG) can identify PVCs. Because PVCs tend to be intermittent, the doctor may use a Holter monitor ECG, which records the heart's electrical activity over a period of 24 hours.

Unless PVCs indicate a serious underlying arrhythmia, cardiologists usually do not treat them. Often, eliminating potential causes such as caffeine can put an end to the PVCs. The cardiologist may

prescribe a beta blocker for persistent PVCs, after ruling out other cardiovascular conditions.

See also ECTOPIC BEAT; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; PALPITATIONS; SMOKING AND HEALTH.

pulmonary arteries The large BLOOD vessels that carry blood from the HEART to the LUNGS. The main pulmonary ARTERY arises from the right ventricle and immediately branches into the right and left pulmonary arteries. The pulmonary arteries are the only arteries in the body that transport deoxygenated blood. Like other arteries, however, the pulmonary arteries have sturdy, muscular walls that rhythmically contract in synchronization with the heartbeat. The pulmonary valve regulates the flow of blood from the right ventricle into the pulmonary artery.

For further discussion of the pulmonary arteries within the context of cardiovascular structure and function please see the overview section "The Cardiovascular System."

See also AORTA; VALVULAR HEART DISEASE.

pulmonary hypertension Elevated BLOOD PRESSURE in the PULMONARY ARTERIES and the arteries within the LUNGS. Pulmonary HYPERTENSION develops when the arteries in the lungs become stiff and narrowed, increasing the resistance BLOOD encounters in trying to flow through them. The condition typically starts in the smallest of arteries, the arterioles, and progressively involves larger arteries until pressure within the pulmonary arteries from the HEART also rises. Elevated pressure within the pulmonary arteries increases the force the right ventricle must exert to pump blood from the heart to the lungs. Though early in the course of the condition the right ventricle can compensate by enlarging, eventually the increased workload can lead to right HEART FAILURE.

Doctors classify pulmonary hypertension, also called pulmonary arterial hypertension (PAH), as either secondary or primary. Secondary pulmonary hypertension develops as a complication of other health conditions, notably connective tissue disorders and chronic health conditions such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) and PULMONARY EMBOLISM. Because it follows other health conditions that become more likely with advancing age, secondary pulmonary hypertension tends to occur more frequently in people over age 60.

CONDITIONS THAT CAN CAUSE PULMONARY HYPERTENSION

AIDS	CARDIOMYOPATHY
chronic hemolytic ANEMIA	CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)
COCAINE use	HEART FAILURE
OBSTRUCTIVE SLEEP APNEA	PULMONARY EMBOLISM
PULMONARY FIBROSIS	RHEUMATIC HEART DISEASE
scleroderma	SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
VALVULAR HEART DISEASE	

Primary pulmonary hypertension (PPH) exists independently of other health conditions and is far less common than secondary pulmonary hypertension. Most often doctors do not know what causes PPH, though they believe in many people the condition is congenital (present at birth). Though systemic hypertension—what people think of as high blood pressure—may damage blood vessels throughout the body as well as damage the heart, pulmonary hypertension and systemic hypertension are different conditions. PPH can affect people of any age though is more common among people under age 50.

Symptoms and Diagnostic Path

The earliest symptom of pulmonary hypertension is shortness of breath (DYSPNEA), typically with exertion. As the condition progresses, symptoms may include fatigue, SYNCOPE (fainting), chest pressure or PAIN, peripheral edema (swelling of the lower legs, feet, wrists, and hands), ASCITES (fluid retention in the abdominal cavity), and PULMONARY EDEMA (fluid accumulation in the alveoli, or air sacs, in the lungs). Symptoms of advanced disease often include shortness of breath at rest, CYANOSIS (bluish hue to the SKIN and lips), and ARRHYTHMIA (abnormal HEART RATE).

The diagnostic path begins with ELECTROCARDIOGRAM (ECG), which reveals right ventricular hypertrophy (enlargement), and ECHOCARDIOGRAM, which shows the heart's changed structure and function. The right ventricle typically enlarges and its walls thicken as the pulmonary hypertension begins to cause symptoms. Other diagnostic procedures may include MAGNETIC RESONANCE IMAGING (MRI) for additional visualization of the heart, PULMONARY FUNC-

TION TESTS to assess LUNG CAPACITY and the ability of the lungs to exchange oxygen and carbon dioxide, and CARDIAC CATHETERIZATION to measure the pressure within the pulmonary arteries.

Treatment Options and Outlook

Doctors may prescribe medications such as vasodilators and calcium channel blockers to help relax the arteries in the lungs and lower resistance to the flow of blood, anticoagulant medications to lower the risk for blood clots, and diuretics ("water pills") to reduce edema. Research suggests that many people who have pulmonary hypertension have elevated levels of endothelin, an amino acid compound (peptide) naturally present in the walls of the arteries that causes them to constrict. Whether this elevation is a consequence or cause of pulmonary hypertension remains unclear, though its recognition has resulted in the development of medications called endothelin receptor antagonists. These medications relieve the symptoms of pulmonary hypertension by relaxing the walls of the arteries in the lungs. Oxygen therapy can improve the amount of oxygen that enters the blood circulation.

Treatment targets the underlying cause, to the extent possible, when pulmonary hypertension is secondary, as well as aims to lower pulmonary blood pressure. However, any damage that occurs to the heart is generally irreversible. PPH is progressive and as yet there is no curative treatment. Early diagnosis and medications can slow PPH's progression and improve QUALITY OF LIFE. Lifestyle modifications, such as WEIGHT LOSS AND WEIGHT MANAGEMENT, SMOKING CESSATION, and regular physical activity within the capacity the person's cardiovascular function allows, help keep the cardiovascular system functioning as efficiently as possible. LUNG TRANSPLANTATION may be a treatment option for younger people when PPH is the only significant health condition. People who also have severe heart failure may benefit from a combined heart–lung transplantation. These are complex operations, however, and donor organs are extremely limited.

Risk Factors and Preventive Measures

The risk factors for secondary pulmonary hypertension are the conditions that may cause it. Early diagnosis and appropriate treatment for these conditions helps prevent pulmonary hypertension from developing. Because doctors do not know what causes PPH, they cannot identify clear risk factors.

See also CARDIOVASCULAR DISEASE PREVENTION; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; ORGAN TRANSPLANTATION; OXYGEN–CARBON DIOXIDE EXCHANGE.

pulmonary veins The large blood vessels that bring blood to the left side of the HEART from the LUNGS. The main pulmonary veins arise from the lungs and branch immediately into the right pulmonary vein and the left pulmonary vein. The right pulmonary vein carries blood from the right lung and the left pulmonary vein carries blood from the left lung. The pulmonary veins are the only veins in the body that transport oxygenated blood.

For further discussion of the pulmonary veins within the context of cardiovascular structure and function, please see the overview section "The Cardiovascular System."

See also AORTA; VENA CAVA.

pulse The pattern of contractions in the arteries as BLOOD passes through them, typically synchronized with the contractions of the HEART. Where an ARTERY is close to the surface, it is possible to feel the pulse by applying pressure with two fingers (but not the thumb, which has its own perceptible pulse).

PULSE POINTS

Artery	Body Location
abdominal aorta	solar plexus area of the abdomen
brachial	inside of the upper arm
carotid	each side of the neck, below the jaw
femoral	groin
pedal	top of the foot
popliteal	behind the knee
radial	wrist, below the base of the thumb
temporal	side of the forehead
tibial	inside of the lower leg, behind the inner ankle
ulnar	wrist, at the base of the hand on the opposite side from the thumb

ARRHYTHMIAS in which the heart contracts but does not eject blood with the contraction, such as with some tachycardias, may result in a disparity between the pulse and the heart rate. The nature of the pulse aids in diagnosis:

- An ***alternating pulse*** has a regular rhythm though some beats are strong and others are weak. It may suggest left HEART FAILURE.
- A ***bigeminal pulse*** is a pattern of two beats, a strong beat then a weak beat with a long pause after. It suggests PREMATURE VENTRICULAR CONTRACTIONS (PVCS).
- A ***bounding pulse*** may be rapid and forceful. It may indicate HYPERTENSION, FEVER, ANEMIA, or RENAL FAILURE. A bounding pulse also may occur following intense physical exercise, in which case it is normal.
- A ***rapid pulse,*** also called an accelerated pulse, indicates tachycardia (heart rate of 100 beats per minute or faster). It may suggest an arrhythmia, cardiovascular SHOCK, fever, HYPERTHYROIDISM, or CORONARY ARTERY DISEASE (CAD). A rapid pulse also may occur normally following intense physical exercise.
- A ***trigeminal pulse*** is a pattern of two equally strong beats then a third weak beat with a long pause after. It may suggest CARDIOMYOPATHY.
- A ***water-hammer pulse*** is a pattern in which there is a rapid surge of blood at the pulse point followed by a complete collapse of the artery. It suggests aortic regurgitation, a condition in which the aortic valve fails to close after the left ventricle pumps blood into the aorta, allowing blood to flow back into the heart.

The characteristics of the pulse change with fitness level and age. People who exercise regularly and people who are over age 70 tend to have slower pulse rates than people who are sedentary or young. The average resting pulse for an adult is 60 to 100 beats per minute. Children typically have more rapid pulse rates. The pulse rate also temporarily increases with fever, PAIN, and anxiety.

See also BLOOD PRESSURE; HEART SOUNDS; TRADITIONAL CHINESE MEDICINE (TCM).

radiofrequency ablation A therapeutic procedure to treat ARRHYTHMIA disorders such as WOLFF-PARKINSON-WHITE SYNDROME or PAROXYSMAL ATRIAL TACHYCARDIA (PAT). Radiofrequency ablation uses high-frequency energy, similar to microwave energy, to destroy abnormal electrical pathways in the HEART. The cardiologist performs radiofrequency ablation via CARDIAC CATHETERIZATION, threading a catheter through a blood vessel and into the heart. Electrodes on the tip of the catheter function somewhat as an ELECTROCARDIOGRAM (ECG), sending information about the heart's electrical activity via the catheter back to a monitor. When the catheter reaches the area of dysfunctional electrical activity, the cardiologist sends a burst of high-frequency energy through the electrodes. The energy destroys the area of myocardial tissue responsible for the dysfunction, closing the abnormal electrical pathway. The heart's regular electrical pathways then become the route for the heart's electrical pacing impulses. Radiofrequency ablation permanently ends the arrhythmia about 90 percent of the time.

See also ATRIOVENTRICULAR (AV) NODE; IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD); PACEMAKER; SINOATRIAL (SA) NODE.

Raynaud's syndrome A condition in which the smallest arteries, the arterioles, in the hands and the feet spasm in response to cold. The spasm interrupts the flow of BLOOD to the fingers and toes, depriving them of oxygen. Raynaud's syndrome may be idiopathic (without identifiable cause) or secondary to other health conditions (notably connective tissue disorders). Raynaud's syndrome may also develop as a SIDE EFFECT of certain medications such as vasoconstrictors (drugs that cause the blood vessels to constrict). Cigarette smoking is often a precipitating factor and worsens symptoms. Some doctors use the terms *Raynaud's disease* to identify idiopathic Raynaud's and *Raynaud's phenomenon* to identify secondary Raynaud's.

POSSIBLE CAUSES OF RAYNAUD'S SYNDROME

cigarette smoking	dermatomyositis
electrical shock	ergot medications
FROSTBITE or HYPOTHERMIA	long-term exposure to vibration
PERIPHERAL VASCULAR DISEASE (PVD)	REPETITIVE MOTION INJURIES
RHEUMATOID ARTHRITIS	SCLERODERMA
SPINAL CORD INJURY	
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	

The doctor generally makes the diagnosis on the basis of the pattern of symptoms, which is distinctive and consistent. The pattern includes three phases most easily identified according to the color of the fingers or toes:

1. Cold causes the arterioles to spasm, depriving the fingers or toes of oxygen. The fingers or toes turn white.
2. The veins and capillaries dilate, flooding the tissues with deoxygenated blood. The fingers or toes turn blue (CYANOSIS) and typically feel numb.
3. With warmth the arterioles will relax, which restores the flow of circulation and floods the fingers or toes with oxygenated blood. The fingers or toes turn deep red, and may throb and feel hot.

The most effective treatment for Raynaud's syndrome is keeping the fingers and toes warm to prevent the arterioles from spasming. When an attack occurs, warming the fingers or toes gener-

ally restores normal circulation and ends the symptoms. Stress and anxiety may sometimes initiate the symptoms. Relaxation methods such as MEDITATION are helpful when this is the case. BIOFEEDBACK is effective for some people, and regular physical exercise helps maintain circulation. When Raynaud's syndrome fails to respond to preventive and lifestyle measures, doctors may prescribe medications such as beta blockers, calcium channel blockers, or topical nitroglycerin to relax the arterioles. Treating any underlying conditions helps mitigate the symptoms of Raynaud's syndrome.

See also MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; NEUROPATHY; PULMONARY HYPERTENSION; SMOKING AND CARDIOVASCULAR DISEASE.

risk factors for cardiovascular disease The circumstances that make a person more or less likely to develop conditions affecting the HEART and cardiovascular system. A risk factor may be fixed, or immutable, such as age, ethnicity, or gender. Other risk factors are variable, or mutable. These are the risk factors that an individual can influence, such as dietary habits and physical activity. Doctors also use the terms *alterable* and *nonalterable*, respectively. Other health conditions may also become risk factors for CARDIOVASCULAR DISEASE (CVD), notably DIABETES. Certain cardiovascular conditions, such as HYPERTENSION (high BLOOD PRESSURE) and ATHEROSCLEROSIS, are risk factors for other cardiovascular conditions such as STROKE and HEART ATTACK.

CARDIOVASCULAR DISEASE RISK FACTORS

Fixed	Variable
male	cigarette smoking
age 60 and older	OBESITY
genetic predisposition	physical inactivity
African American heritage	HYPERLIPIDEMIA (elevated blood lipid levels)
Native American heritage	HYPERTENSION (high BLOOD PRESSURE)
female postmenopause	DIABETES

More than 90 percent of cardiovascular disease among Americans develops over decades, the consequence of interactions between genetic predisposition and lifestyle. Health experts believe lifestyle choices can prevent nearly all of such acquired cardiovascular disease, even when there are genetic influences. The HUMAN GENOME PROJECT, the mapping of the human genome, has broadened scientific understanding of genes and of how they influence health and disease. Researchers are better able to assess and even manipulate the interplay between certain genetic factors and lifestyle factors. One area of ongoing genetic research is ethnicity. Though the rate of CVD is significantly higher among people of certain ethnic heritages, the reasons remain unclear.

Though individuals cannot alter genetic predisposition for health conditions, they can often mitigate, through lifestyle, the ways in which such predispositions play out in their lives. A person who has a family history of early-onset atherosclerosis, for example, may mitigate the effects of this genetic predisposition through daily moderate exercise (aerobic and STRENGTH) and dietary habits that limit fat consumption to less than 10 percent of daily calories and increased fiber consumption, as well as through maintaining healthy body weight. Other preventive measures may include frequent blood lipid level screening (every 6 to 12 months) and lipid-lowering medications for lipid levels that remain elevated despite lifestyle efforts to keep them low. These lifestyle efforts can minimize, and often prevent, cardiovascular disease.

An important dimension to risk factors for CVD is the interplay that exists among them. Physical inactivity is a key element in the development and progression of HYPERLIPIDEMIA, type 2 DIABETES, OBESITY, and hypertension. Hyperlipidemia lays the foundation for atherosclerosis, which progresses to CORONARY ARTERY DISEASE (CAD). CAD causes ISCHEMIC HEART DISEASE (IHD) and is the leading cause of heart attack. Hypertension, alone though especially in combination with atherosclerosis (CAD or PVD), is the leading cause of stroke.

Congenital heart conditions, even those repaired in early childhood, may predispose people to other forms of cardiovascular disease later in life. Adults under age 30 are the first generation for whom surgical correction of congenital heart defects was a viable treatment option. Doctors do not yet know the extent to which these anomalies may affect future cardiovascular risk.

Many health experts question whether the risk of age is more a reflection of cumulative variable risks than itself an independent risk factor. Targeting individual risk factors early in life, before substantial cardiovascular disease develops, is the most effective preventive measure. Once a cardiovascular condition begins, preventive efforts shift focus to slow the progression of disease.

See also CALORIE; CARDIOVASCULAR DISEASE PREVENTION; DIET AND CARDIOVASCULAR HEALTH; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; SMOKING AND CARDIOVASCULAR DISEASE.

rheumatic heart disease Damage to the valves of the HEART as a consequence of rheumatic FEVER, which develops as a complication of untreated or undertreated STREP THROAT. Streptococcal BACTERIA attack the heart valves, most commonly the mitral and aortic valves, which can leave them scarred and deformed. Rheumatic fever and rheumatic heart disease are now uncommon as ANTIBOTIC MEDICATIONS so successfully treat strep infections involving the THROAT. In the 1950s rheumatic heart disease was the leading cardiovascular cause of disability and death among American adults. Today, rheumatic heart disease is much less of a threat though still affects about 2 million Americans each year, about 3,500 of whom die as a result.

Signs of CARDIOVASCULAR DISEASE (CVD) that suggest rheumatic heart disease may include clinically significant HEART MURMUR and other indications of valvular insufficiency. Doctors may suspect rheumatic heart disease as the cause when there is a recent history of sore throat or strep throat in combination with symptoms that suggest autoimmune or inflammatory disease, such as inflamed joints, and of cardiac insufficiency, such as DYSPNEA (shortness of breath). The diagnostic path typically includes ELECTROCARDIOGRAM (ECG) to evaluate any arrhythmias, which are common in VALVULAR HEART DISEASE. ECHOCARDIOGRAM or MAGNETIC RESONANCE IMAGING (MRI) allows the cardiologist to visualize and assess the heart's valves, structure, and function.

Treatment for rheumatic heart disease may involve medications to treat secondary cardiovascular conditions such as arrhythmias and HEART FAILURE, and surgical repair or replacement of damaged valves. People who have rheumatic heart disease are vulnerable to subsequent infections and require ANTIBIOTIC PROPHYLAXIS before invasive diagnostic and therapeutic procedures, and with infections such as PHARYNGITIS, to prevent ENDOCARDITIS.

See also AUTOIMMUNE DISORDERS; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; SCARLET FEVER.

S

sexual activity and cardiovascular disease HEART ATTACK, STROKE, major HEART surgery such as CORONARY ARTERY BYPASS GRAFT (CABG) or HEART TRANSPLANTATION, or the diagnosis of a cardiovascular condition such as HYPERTENSION (high BLOOD PRESSURE) or CORONARY ARTERY DISEASE (CAD) often causes worry and fear that sexual activity may harm the heart. Such concerns are common though generally have no medical basis. Sexual intercourse requires about the same level of cardiovascular response from the body as walking up three flights of stairs. Following a cardiovascular event, most people may resume sexual activity when they regain interest.

These preparations may make the return to sexual activity more enjoyable:

- Plan sexual activity for when both partners are well rested, relaxed, and have no time constraints.
- Plan sexual activity to take place two to three hours after eating a meal, to allow digestion to take place. Digestion diverts more of the body's blood supply to the gastrointestinal tract.
- Choose a location that is comfortable and free from distractions such as the telephone or interruptions.
- Choose less strenuous positions and have extra pillows available for added support.
- Be patient and focus on the intimacy of being together.

People who have had OPEN HEART SURGERY or who have residual complications resulting from stroke may feel unsure of their physical attractiveness. Open, honest communication between partners can help put these concerns in perspective and allow each partner to express his or her feelings.

See also LIVING WITH CARDIOVASCULAR DISEASE; QUALITY OF LIFE.

sick sinus syndrome A collective term for ARRHYTHMIA disorders that arise from dysfunction of the SINOATRIAL (SA) NODE and the electrical conduction network within the HEART. The SA node may stop functioning, or there may be a disruption in the pathway for the electrical impulses the SA node generates. Generally sick sinus syndrome results in bradycardia (slow HEART RATE). Key symptoms include fatigue and SYNCOPE (fainting). Sick sinus syndrome may also be present without symptoms, in which case it does not usually require treatment. ELECTROCARDIOGRAM (ECG) reveals the abnormal electrical pacing impulses and provides the diagnosis. Treatment is nearly always an implantable PACEMAKER to maintain an adequate heart rate.

See also ATRIOVENTRICULAR (AV) NODE; BUNDLE BRANCH; BUNDLE BRANCH BLOCK; LONG QT SYNDROME (LQTS); WOLFF-PARKINSON-WHITE SYNDROME.

sinoatrial (SA) node A small cluster of specialized NERVE and MUSCLE fibers located in the upper wall of the heart's right atrium. The SA node initiates the electrical pacing impulse that causes the HEART to contract. In the healthy heart the electrical impulse spreads in an orderly and synchronized pattern through the two atria, causing them to contract. The ATRIOVENTRICULAR (AV) NODE, a second small cluster of specialized nerve and muscle fibers located in the wall of the heart between the atria and the ventricles, picks up the impulse, amplifies it, and sends it through the ventricles to cause them to contract.

For further discussion of the SA node within the context of cardiovascular structure and function please see the overview section "The Cardiovascular System."

See also BUNDLE BRANCH; BUNDLE BRANCH BLOCK; CARDIAC CYCLE; SICK SINUS SYNDROME.

smoking and cardiovascular disease CARDIOVASCULAR DISEASE (CVD) is the most frequent and significant consequence of cigarette smoking, with smoking accounting for one in six deaths due to CVD. Smoking significantly increases the risk for HYPERTENSION (high BLOOD PRESSURE), ATHEROSCLEROSIS, and CORONARY ARTERY DISEASE (CAD). The combination of cigarette smoking and using oral contraceptives (birth control pills) presents a particular risk of BLOOD clot formation in women, especially women over age 35. This raises the risk for STROKE and HEART ATTACK such that many doctors will not prescribe oral contraceptives for women who smoke. Smoking is also a key factor in numerous pulmonary diseases, affecting the cardiovascular system's ability to circulate oxygen-rich blood.

The US Surgeon General offered the first conclusive evidence of the correlations between smoking and cardiovascular disease in the landmark 1964 report, *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service*. Researchers have since continued to accumulate knowledge and understanding of the mechanisms through which smoking affects cardiovascular health. Cigarette smoke contains more than 2,000 identifiable chemicals, dozens of which are carcinogenic (CANCER-causing) or have other deleterious actions on health. Two in particular, NICOTINE and carbon monoxide, are highly toxic to the cardiovascular system.

Nicotine and Cardiovascular Function

NICOTINE is a CENTRAL NERVOUS SYSTEM stimulant that acts on nerves throughout the body. In the cardiovascular system, nicotine stimulates the nerves that regulate smooth MUSCLE tissue, causing smooth muscle cells to contract. This constricts blood vessels, notably arteries, reducing the channel for blood flow. Nicotine further stimulates the baroreflex sensors (clusters of NERVE cells in the major arteries and the heart that sense the flow and pressure of blood). These actions result in increased blood pressure, HEART RATE, and cardiac workload. Nicotine further acts as an irritant within the arteries, causing INFLAMMATION of the inner layer of the arterial wall. Researchers believe such inflammation may be the foundation for atherosclerosis.

Carbon Monoxide and Cardiovascular Function

Carbon monoxide is a poison. It has a greater affinity than oxygen for HEMOGLOBIN and binds with hemoglobin, blocking hemoglobin from carrying oxygen. This reduces the amount of oxygen that enters the bloodstream from the LUNGS. By the end of a cigarette, a smoker can have concentrations of carbon monoxide as high as 7 percent; 10 percent is the level at which symptoms of carbon monoxide poisoning begin to become apparent. Carbon monoxide in the bloodstream deprives cells in the BRAIN and heart, which rely on oxygen for fuel.

Environmental Smoke Exposure

Cigarette smoke also raises the risk for health problems, including cardiovascular disease, among people who are themselves nonsmokers though live or work in a smoking environment. Children are at particular risk. Numerous studies show the children of smokers have more EAR infections, sinus infections, and upper respiratory infections than children who live in smoke-free environments. Long-term exposure to ENVIRONMENTAL CIGARETTE SMOKE, called passive smoking, has the same health consequences as active smoking.

Smoking Cessation

The health risks of cigarette smoking diminish within 30 to 40 minutes of the last puff. With sustained SMOKING CESSATION, the risk for cardiovascular disease gradually diminishes over 5 to 10 years, finally reaching a level consistent with the risks for a nonsmoker. Any damage that has already occurred to the cardiovascular system is permanent, however.

See also ANTISMOKING EFFORTS; CARDIOVASCULAR DISEASE PREVENTION; CONTRACEPTION; HEALTH RISK FACTORS; INHALED TOXINS; LIFESTYLE AND CARDIOVASCULAR HEALTH; SMOKING AND CANCER; SMOKING AND HEALTH.

soy and cardiovascular health Soy protein appears to help lower cholesterol blood levels, particularly low-density lipoprotein cholesterol (LDL-C). The American Health Association recommends replacing animal protein with soy protein as part of a balanced, low-fat diet. People who consume 25 to 50 grams of soy protein daily can lower their LDL-C levels by as much as 8 percent. In combination with other cholesterol-lowering approaches such as increased daily exercise, soy in the diet contributes to a heart-healthy lifestyle. Soy protein contains isoflavones—notably genistein, daidzein, and glycetein—that help to reduce the formation of ATHEROSCLEROTIC PLAQUE, thus lowering the risk for ATHEROSCLEROSIS and related conditions such as CORONARY ARTERY DISEASE (CAD). Soy protein is also high in fiber, helping absorb dietary cholesterol and fats in the intestinal tract to reduce the amount that enters the blood circulation.

DIETARY SOURCES OF SOY PROTEIN

soy cheese	soy flour
soybeans (boiled or roasted)	soy milk
textured vegetable protein (TVP) products	tofu

See also CARDIOVASCULAR DISEASE PREVENTION; DIET AND CARDIOVASCULAR HEALTH; HORMONE-DRIVEN CANCERS; LIFESTYLE AND CARDIOVASCULAR HEALTH.

stent A tiny, springlike device inserted into an ARTERY to help maintain the artery's patency after ANGIOPLASTY (a CARDIAC CATHETERIZATION procedure to clear or compress ATHEROSCLEROTIC PLAQUE from the inner walls of an artery). The stent holds pressure against the artery's inner wall, maintaining compression of the plaque as well as making it difficult for the artery to constrict. Cardiologists use stents primarily in the CORONARY ARTERIES though may also use them in carotid ENDARTERECTOMY and peripheral artery angioplasty. An anticoagulant medication coats some stents, called DRUG-emitting, to discourage clot formation. Stents can extend the effectiveness of angioplasty by months to a year or more. Angioplasty with stent placement can delay the need for CORONARY ARTERY BYPASS GRAFT (CABG) or provide an acceptable alternative for people with less severe occlusions. Most stents require replacement every three to five years.

See also ANTICOAGULATION THERAPY; BLOOD; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE.

stethoscope An instrument the doctor uses to listen to sounds within the body. The cardiologist uses a stethoscope to listen to the function of the valves in the HEART, to the HEART RATE, to the flow of BLOOD through the chambers of the heart, and for abnormal sounds, such as a pericardial rub or a HEART MURMUR, that can indicate cardiovascular disorders. The French physician René Laënnec (1781–1821) invented the stethoscope and introduced the first practical model, a simple tube with a flare at one end and a small opening that served as an earpiece at the other end, in 1816. The instrument evolved over the next 100 years into the familiar style in use today, a flexible "Y" of tubing with dual earpieces and a combination bell and diaphragm with a lever to switch between them. The bell picks up low-pitched tones and the diaphragm picks up high-pitched tones.

See also AUSCULTATION.

stress test A diagnostic procedure to evaluate the cardiovascular system's ability to meet the body's increased oxygen needs during physical exercise. The most common procedure is the exercise stress test, in which the person walks on a treadmill or rides a stationary bicycle at an escalating pace. A continuous ELECTROCARDIOGRAM (ECG) monitors the heart's response. Variations of the stress test include the ECHOCARDIOGRAM stress test, in which the cardiologist uses ULTRASOUND to visualize the heart's functions during exercise, and the pharmacological stress test, in which the cardiologist administers a DRUG such as dipyridamole that causes a cardiovascular response that simulates the effects of exercise. A stress test helps determine the extent of cardiovascular impairment present as a result of conditions such as CORONARY ARTERY DISEASE (CAD) and HEART FAILURE. A stress test does not require preparation or recovery, and takes 20 to 40 minutes to complete. There is a very slight risk that a stress test may trigger a HEART ATTACK, to which the facility and its staff are prepared to respond if necessary.

See also HEART; MYOCARDIAL PERFUSION IMAGING; OXYGEN–CARBON DIOXIDE EXCHANGE.

stroke An interruption of BLOOD flow and oxygen supply to the BRAIN, sometimes called a brain attack. Stroke strikes about 700,000 Americans each year. For two thirds of them the stroke is a second or subsequent stroke. About 85 percent of strokes are ischemic; they result from blockage of an arterial pathway in the brain. The remaining 15 percent are hemorrhagic; they result from bleeding into the brain, typically from a blood vessel that ruptures. About 90 percent of people survive a first ischemic stroke, though a third of them experience permanent disability of varying severity as a consequence of the damage to the brain. The risk for death rises with each subsequent stroke. Hemorrhagic strokes are more likely to be fatal, claiming the lives of nearly half of those who have them. In 2000, about 2.4 million Americans were stroke survivors.

HYPERTENSION (high BLOOD PRESSURE) is the leading cause of stroke. Unfortunately, hypertension has no symptoms and many people do not know they have it until they suffer stroke or HEART ATTACK. Chronically elevated blood pressure stresses blood vessels, causing them to stiffen and thicken to help protect against the constant pounding of blood. This response (ARTERIOSCLEROSIS) makes the arteries vulnerable to INFLAMMATION and accumulations of debris (ATHEROSCLEROTIC PLAQUE), resulting in ATHEROSCLEROSIS. The high pressure of blood rushing through the arteries causes tiny fragments of the plaque to break free. The fragments float through the blood circulation until they lodge in a blood vessel, blocking the further flow of blood. When this occlusion happens in the heart, it causes a MYOCARDIAL INFARCTION or heart attack. In the brain, the occlusion causes stroke.

Health experts recommend annual BLOOD PRESSURE checks for all people age 50 and older, and for younger people who have risk factors for CARDIOVASCULAR DISEASE (CVD).

Brain cells require a constant supply of oxygen to meet their energy needs. Deprivation of oxygen for as little as 30 seconds causes them to begin shutting down. Lack of oxygen for two to three minutes causes brain cells to begin dying. After five minutes, enough brain cells can die to cause permanent loss of function in the affected area. This loss may involve cognitive function, memory, speech and language processing, and physical movement. The brain's correlation to the body is ipsilateral. Damage to the right brain may result in weakness or paralysis on the left side of the body; damage to the left brain may affect the right side of the body.

Time is crucial. Treatment for ischemic stroke that begins within four hours can incorporate drugs to dissolve the blocking blood clot, minimizing or preventing damage to the brain.

Symptoms and Diagnostic Path

Symptoms of stroke may be subtle or pronounced. The main symptoms of stroke include

- numbness or tingling on one side of the face or body
- difficulty speaking (including slurred speech) or swallowing
- drooping of facial features on one side
- weakness or PARALYSIS on one side of the body
- loss of vision or change in vision, particularly in only one EYE

It is important to seek medical attention without delay at the first indication that a stroke may be occurring. Early treatment with THROMBOLYTIC THERAPY can dissolve developing blood clots, mitigating or preventing the stroke. The diagnostic path typically includes COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to visualize the location and extent of the stroke, and to determine whether the stroke is ischemic or hemorrhagic. ELECTROENCEPHALOGRAM (EEG), which measures the brain's electrical activity, and a comprehensive NEUROLOGIC EXAMINATION can help assess the extent of damage the stroke has caused.

Treatment Options and Outlook

Immediate treatment focuses on minimizing damage to the brain. Optimally, early intervention permits thrombolytic therapy, which must begin within four hours of the stroke's onset. Treatment

beyond this window of opportunity typically includes ANTICOAGULATION THERAPY for ischemic stroke to prevent further clots from forming and supportive measures to maintain cardiovascular stability. Most people who experience strokes have hypertension, so subsequent treatment includes measures to bring blood pressure under control through medications and lifestyle changes.

People who receive thrombolytic therapy often have no residual effects from their strokes and can return to their regular activities within a few weeks. People who experience permanent disability as a result of stroke may require inpatient or outpatient rehabilitation. The level of recovery depends on the extent of damage. Many people with serious disabilities are able to learn methods for adapting to their limitations, allowing them to return to some activities and perhaps independent living. About 70 percent of people who experience strokes are able to return to functional independence and often many of their regular activities, within three to six months.

Risk Factors and Preventive Measures

The key risk factors for stroke are hypertension and atherosclerosis. Cardiovascular conditions involving clot formation present a high risk for stroke. These include DEEP VEIN THROMBOSIS (DVT), ATRIAL FIBRILLATION, CAROTID STENOSIS, and VALVULAR HEART DISEASE. DIABETES also raises the risk for stroke. Other risk factors are those for all forms of CARDIOVASCULAR DISEASE (CVD): smoking, physical inactivity, and diet high in saturated fats and excessive calories. Stroke also becomes more likely with advancing age.

The most effective preventive measure is maintaining a healthy blood pressure. All adults over age 50 should have annual blood pressure checks, with more frequent checks when blood pressure is elevated or risk factors for hypertension are present. Efforts to maintain good cardiovascular health, such as daily physical exercise and WEIGHT LOSS AND WEIGHT MANAGEMENT, help lower the risk for subsequent stroke as well as for other forms of cardiovascular disease.

See also CALORIE; CARDIOVASCULAR DISEASE PREVENTION; COGNITIVE FUNCTION AND DYSFUNCTION; ENDARTERECTOMY; HEALTH RISK FACTORS; RISK FACTORS FOR CARDIOVASCULAR DISEASE; SPEECH DISORDERS; SWALLOWING DISORDERS; TRANSIENT ISCHEMIC ATTACK (TIA).

sudden cardiac death Unexpected, fatal CARDIAC ARREST (cessation of cardiac activity). Typically there are no warning signs of impending cardiovascular crisis. Electrical dysfunction is the most frequent cause of sudden cardiac death. In young people, ARRHYTHMIA disorders such as LONG QT SYNDROME (LQTS) or WOLFF-PARKINSON-WHITE SYNDROME, or hereditary HEART conditions such as hypertrophic CARDIOMYOPATHY, are often to blame. Some health experts believe ELECTROCARDIOGRAM (ECG) should be a part of the athletic physical examination, as intense physical exertion can trigger electrical dysfunctions that result in death.

In people age 50 and older sudden cardiac death typically results from arrhythmia disorders, MYOCARDIAL INFARCTION, ISCHEMIC HEART DISEASE (IHD) that is a consequence of CORONARY ARTERY DISEASE (CAD), and HEART FAILURE. Most people who experience sudden cardiac death were unaware they had CARDIOVASCULAR DISEASE (CVD) or had been undergoing successful treatment to manage a particular cardiovascular condition such as HYPERTENSION. Because the event that causes cardiovascular collapse is generally catastrophic, resuscitative efforts tend to be unsuccessful.

See also CARDIOPULMONARY RESUSCITATION (CPR); CARDIOVASCULAR DISEASE PREVENTION; HEALTH RISK FACTORS; MARFAN SYNDROME; TORSADE DE POINTES.

syncope The temporary loss of CONSCIOUSNESS and posture, commonly called fainting. Syncope is common and can arise from numerous causes ranging from standing too long, which allows BLOOD to pool in the legs, to ARRHYTHMIA and TRANSIENT ISCHEMIC ATTACK (TIA), which interrupt the flow of blood to the BRAIN. About 10 percent of syncope episodes are the result of cardiovascular events such as arrhythmias, MYOCARDIAL INFARCTION, MICROINFARCTION, HYPOTENSION, and TIA.

Any episode of syncope in a person who has a history of HEART ATTACK, STROKE, ARRHYTHMIA, or other known CARDIOVASCULAR DISEASE (CVD) requires immediate medical evaluation.

Other causes of syncope include neurologic events (such as vasovagal response), medication side effects, heat, DEHYDRATION, fear, FEVER, and PREGNANCY. Most people regain consciousness within a few seconds to three minutes. Syncope may be an isolated event or a symptom of underlying health concerns. A doctor should evaluate recurrent episodes of syncope. Such an evaluation typically includes a NEUROLOGIC EXAMINATION and an ELECTROCARDIOGRAM (ECG).

See also ADVERSE REACTION; CRANIAL NERVES; GASTROPARESIS; SEIZURE DISORDERS; UNCONSCIOUSNESS.

T

tachycardia See ARRHYTHMIA.

tamponade, cardiac A life-threatening compression of the HEART that prevents it from expanding to fill with BLOOD. Cardiac tamponade is most often a complication of PERICARDITIS and develops when fluid rapidly accumulates within the layers of the PERCARDIUM. The pericardium's fibrous outer layer does not readily expand, which forces the fluid to press inward against the heart. Without immediate action to drain the fluid, the heart will stop beating. ELECTROCARDIOGRAM (ECG) demonstrates the characteristic patterns of electrical changes in the heart's rhythm that strongly indicate cardiac tamponade. COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) can confirm the diagnosis. Generally the doctor can aspirate (withdraw) the fluid using a needle and syringe (pericardiocentesis), which relieves the pressure and allows the heart to resume normal function. Surgery to create an opening in the pericardium may be necessary to manage cardiac tamponade that occurs with chronic pericarditis. Penetrating trauma that causes bleeding into the pericardium may also cause cardiac tamponade.

See also MYOCARDIAL INFARCTION.

thrombolytic therapy Emergency treatment with medications to dissolve BLOOD clots that are in the process of forming. When initiated promptly, thrombolytic therapy can avert MYOCARDIAL INFARCTION or ischemic (nonhemorrhagic) STROKE, mitigating damage to the HEART or BRAIN respectively. Doctors also may use thrombolytic therapy to treat blood clots that form elsewhere in the body, such as in the leg (DEEP VEIN THROMBOSIS [DVT]) or the LUNGS (PULMONARY EMBOLISM).

Thrombolytic agents act by converting plasminogen, an inactive protein in the blood circulation, to plasmin, an active protein that breaks down the key proteins that form blood clots (fibrinogen and fibrin). These agents can only act before the clot fully forms and hardens, which establishes a therapeutic window of about four hours from the onset of clot formation. Early diagnosis is therefore essential.

COMMON THROMBOLYTIC AGENTS

alteplase (aPA)	anisoylated purified streptokinase activator complex (APSAC)
anistreplase	streptokinase
tissue plasminogen activator (tPA)	urokinase

The oldest of the thrombolytic agents is streptokinase, which doctors began using in the 1940s. Streptokinase and anistreplase derive from streptococcal BACTERIA. When administered, these agents initiate ANTIBODY production. The antibodies become active after five days and remain active for about six months. During that timeframe, doctors cannot re-administer streptokinase or anistreplase. Some people also have adverse responses to these agents, especially streptokinase. Laboratories manufacture most of the newer thrombolytic agents using recombinant technology, which nearly eliminates these immune responses.

The most significant risk of thrombolytic therapy is uncontrolled bleeding (HEMORRHAGE). For this reason, it is crucial for doctors to determine whether a stroke is ischemic (caused by a clot) or hemorrhagic (caused by bleeding) before administering a thrombolytic agent. For venous clots, such as with deep vein thrombosis, the doctor may directly inject the agent into the clot. For arterial

clots, such as with myocardial infarction or stroke, the doctor injects the agent into a vein for distribution throughout the circulation. Thrombolytic agents remain active in the bloodstream for 15 to 90 minutes, depending on the agent. With prompt initiation of thrombolytic therapy, the agent dissolves the clot and the person experiences little or no adverse effects as a consequence of the thrombolytic event.

See also ANTICOAGULANT THERAPY; IMMUNE RESPONSE.

torsade de pointes A life-threatening ventricular tachycardia (rapid contractions of the ventricles) that is the most serious complication of the ARRHYTHMIA disorder LONG QT SYNDROME (LQTS). Torsade de pointes is a distinctive pattern of QRS complex electrical activity, QRS being the points on the ELECTROCARDIOGRAM (ECG) that identify ventricular contraction.

The term "torsade de pointes" means "twisting around the points." In ballet, the term's origination, the term identifies a movement in which multiple steps rotate the dancer around an imaginary axis. On the ECG, the QRS complex appears to twist around the electrical baseline with a continuously changing point of origin, reminiscent of the ballet movement. The pattern represents a progressive change in myocardial cell polarity (abnormal shifts in the cell's electrical charge), a marked dysfunction of the heart's electrical pacing and conduction mechanisms. Unless interrupted, torsades de pointes results in SUDDEN CARDIAC DEATH.

The ECG provides definitive diagnosis. Torsade de pointes may stop spontaneously or may require emergency medical intervention such as DEFIBRILLATION (electrical shock to restore normal rhythm) or a temporary PACEMAKER. Numerous medications can cause acquired LQTS and consequently torsade de pointes, including the commonly prescribed antibiotic erythromycin, ANTIPSYCHOTIC MEDICATIONS such as the phenothiazines, and most drugs that affect the heart's function such as those to treat arrhythmias, HEART FAILURE, and HYPERTENSION (high BLOOD PRESSURE). COCAINE also can cause torsade de pointes. Stopping the causative DRUG typically ends the torsade de pointes.

See also HEART; HYPOCALCEMIA; HYPOKALEMIA; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE.

transient ischemic attack (TIA) A brief, episodic interruption of the flow of BLOOD to the BRAIN, often called a mini-STROKE. The most common cause of a TIA is a fragment of ATHEROSCLEROTIC PLAQUE or a BLOOD clot that breaks free and travels through the blood circulation until it lodges in an ARTERY or arteriole. TIAs also can be hemorrhagic, the result of small ruptures in the tiny arteries in the brain, often a consequence of untreated HYPERTENSION (high BLOOD PRESSURE) and CAROTID STENOSIS (narrowing and occlusion of the carotid artery in the neck). ATRIAL FIBRILLATION and VALVULAR HEART DISEASE are other common sources of clots.

Symptoms of TIA are brief and temporary and may include

- episodes of SYNCOPE (loss of CONSCIOUSNESS) or "freezing," in which the person appears conscious and alert but does not respond
- episodes of tingling or numbness affecting the face or parts of the body such as the fingers or hand, typically only on one side of the body
- temporary inability to use the arm or leg, or both, on one side of the body
- lapses in cognitive function or memory

TIAs are more common in people over age 70. Doctors generally consider them to be warning signs of impending stroke. Early diagnosis and therapeutic intervention can help avert full-fledged stroke. The diagnostic path typically includes imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI). Treatment may include ANTICOAGULATION THERAPY to reduce the blood's tendency to clot as well as medications to treat arrhythmias (notably atrial fibrillation), hypertension, and HYPERLIPIDEMIA (elevated blood lipid levels), if these conditions are present. The cardiologist may recommend carotid ENDARTERECTOMY when carotid stenosis is a causative factor.

See also ARRHYTHMIA; CARDIOVASCULAR DISEASE PREVENTION; COGNITIVE FUNCTION AND DYSFUNCTION; MICROINFARCTION.

transmyocardial laser revascularization (TMLR) A treatment for ANGINA PECTORIS and ISCHEMIC HEART DISEASE (IHD) in which the cardiovascular surgeon

uses a laser to create several dozen tiny channels through the wall of the heart's left ventricle to improve the flow of BLOOD and oxygen to the MYOCARDIUM (heart MUSCLE). The surgeon makes a small "window" incision through the ribs to gain access to the myocardium, and the HEART continues to beat during the surgery. The channels allow blood to flow directly from the ventricle's chamber to the muscle tissue. Researchers do not know why TMLR relieves angina pectoris, though believe it allows oxygen to directly enter myocardial cells and also encourages new blood vessels to grow (collateral circulation). Cardiologists generally use TMLR only when other treatments for angina have failed or are not feasible. Most people stay in the hospital for three to seven days following surgery and are able to return to their regular activities, including work, in four to eight weeks.

See also CORONARY ARTERY BYPASS GRAFT (CABG); SURGERY BENEFIT AND RISK ASSESSMENT.

triglycerides blood level The amount of the fatty acid group, triglycerides, that is present in the BLOOD circulation. Most of the body's fats are in the chemical form of triglycerides, which provide the body with energy. The cells draw triglycerides from the blood to meet their immediate energy needs. The body acquires triglycerides from dietary sources as well as manufactures them. During digestion the gastrointestinal tract extracts triglycerides from dietary saturated fats such as are abundant in meats. When the level of triglycerides in the blood meets or exceeds the body's needs, the LIVER converts excess CALORIES that derive from any dietary source into triglycerides. The body stores excess triglycerides in fat cells, drawing from these stored energy supplies when demand, such as increased physical activity, exceeds the triglycerides available in the blood circulation.

In general, blood triglyceride levels rise when CHOLESTEROL BLOOD LEVELS, and particularly low-density lipoprotein cholesterol (LDL-C), are elevated. Blood triglyceride levels also tend to be elevated in OBESITY and DIABETES. The role elevated blood triglyceride levels play in CARDIOVASCULAR DISEASE (CVD) remains unclear. The National Cholesterol Education Program (NCEP), a consensus group of health experts, has established healthy and unhealthy levels of triglycerides in the blood based on correlations between elevated levels and cardiovascular conditions such as ATHEROSCLEROSIS, CORONARY ARTERY DISEASE, (CAD), and PERIPHERAL VASCULAR DISEASE (PVD), as people who have these conditions typically have elevated blood triglycerides as well.

Doctors recommend lifestyle modifications such as reducing dietary saturated fat and ALCOHOL consumption, increased daily exercise, and WEIGHT LOSS AND WEIGHT MANAGEMENT when triglyceride levels are slightly elevated (marginal) and often prescribe lipid-lowering medications when triglyceride levels are high or very high. Some people have elevated triglyceride blood levels and healthy cholesterol blood levels. For them, doctors recommend vigilance to maintain healthy cholesterol blood levels and annual monitoring, along with lifestyle habits that support overall cardiovascular health.

TRIGLYCERIDE BLOOD LEVELS (MILLIGRAMS PER DECILITER)

less than 150 mg/dL	healthy
150 to 199 mg/dL	marginal
200 to 499 mg/dL	high
500 mg/dL or higher	very high

See also CALORIE; DIET AND CARDIOVASCULAR HEALTH; DIET AND HEALTH; HYPERLIPIDEMIA; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; NUTRIENTS.

V–W

valvular heart disease The collective term for the malformations and disorders that can affect the valves of the HEART. Valvular heart disease may affect any of the heart's four valves: mitral, pulmonary, aortic, and tricuspid. The most common forms of valvular heart disease are

- stenosis, in which the valve does not open completely
- regurgitation, also called incompetence or insufficiency, in which the valve does not close completely
- prolapse, affecting primarily the mitral valve, in which the valve leaflets are irregularly shaped such that they bulge when they close

POSSIBLE CAUSES OF VALVULAR HEART DISEASE

ANKYLOSING SPONDYLITIS	atrial septal defect (ASD)
bicuspid aortic valve	calcification
CONGENITAL ANOMALY	CORONARY ARTERY DISEASE (CAD)
ENDOCARDITIS	GRAVES'S DISEASE
HEART ATTACK	hypertrophic CARDIOMYOPATHY
MARFAN SYNDROME	MUSCULAR DYSTROPHY
PULMONARY HYPERTENSION	RHEUMATIC HEART DISEASE
RHEUMATOID ARTHRITIS	SICKLE CELL DISEASE
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	ventricular septal defect (VSD)

Until the 1950s, valvular heart disease was the leading cardiovascular cause of death, and RHEUMATIC HEART DISEASE, a complication of streptococcal INFECTION such as STREP THROAT, was the most frequent cause of valvular heart disease. As ANTIBIOTIC MEDICATIONS became the standard of treatment for strep throat and other infections, rheumatic heart disease and correspondingly valvular heart disease declined dramatically. Though rheumatic heart disease still accounts for about half of valvular heart disease, other causes include congenital malformations and degenerative effects that accompany aging.

Symptoms and Diagnostic Path

Many people who have valvular heart disease do not have symptoms until damage to the heart becomes significant, progressing to HEART FAILURE, CARDIOMYOPATHY, and ARRHYTHMIA. When symptoms are present, they may include

- tiredness or fatigue
- shortness of breath, especially with exertion
- periods of lightheadedness
- chest tightness or discomfort
- PALPITATIONS

Often, the underlying valve malformation (congenital or acquired) exists for years to decades before affecting the valve's function to the extent of causing symptoms. Sometimes the doctor detects valvular heart disease before symptoms are present, commonly by hearing a HEART MURMUR during a ROUTINE MEDICAL EXAMINATION. Though many heart murmurs are occasional and innocent (not indicating any disease), certain valve disorders produce distinctive murmurs. Other procedures likely along the diagnostic path include ELECTROCARDIOGRAM (ECG), ECHOCARDIOGRAM, and COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI). Depending on the person's general cardiovascular status, the cardiologist may also recommend CARDIAC CATHETERIZATION.

Treatment Options and Outlook

Medications can control much valvular heart disease. Those commonly prescribed include antico-

agulants to reduce the risk for blood clots and beta blockers or calcium channel blockers to lower BLOOD PRESSURE and slow the HEART RATE. When heart failure or cardiomyopathy is also present, the cardiologist may prescribe digoxin to strengthen the heart's contractions and diuretic medications to reduce or prevent excessive fluid accumulation in the body tissues. Lifestyle efforts, such as nutritious EATING HABITS and daily physical exercise, are important to improve overall cardiovascular status. SMOKING CESSATION and weight loss, if appropriate, are essential to reduce the risk for further CARDIOVASCULAR DISEASE (CVD).

Surgery becomes a treatment option when medical efforts are unsuccessful or valve damage is significant. Surgical options include repair (valvuloplasty) or replacement (prosthetic valve).

Valvuloplasty Balloon valvuloplasty is a procedure to treat stenosis in which the cardiologist uses cardiac catheterization to thread a catheter with a tiny balloon on the tip through a blood vessel and into the heart. When the catheter tip is in position in the valve's opening, the cardiologist inflates the balloon to gently expand the opening. Operative valvuloplasty involves OPEN HEART SURGERY to gain access to the diseased valve. The surgeon may use various methods to repair the valve, depending on the valve and the nature of the damage.

Valve replacement The surgeon may replace a damaged valve that is beyond repair. Prosthetic heart valves fall into two general categories, tissue and mechanical. Tissue valves come from human cadaver donors or animal tissues. Animal valves are typically porcine (pig) or bovine (cow) and are sterilized and processed before use. The advantage to tissue valves is that they function in the same manner as the native valve. The disadvantage is that they wear out. Mechanical valves are made of materials such as stainless steel and high-tech plastics. Their main advantage is that they are completely inert and last a very long time. After receiving a prosthetic heart valve the person must take ANTICOAGULATION THERAPY for life and take prophylactic antibiotics before invasive dental, surgical, or diagnostic procedures. Prosthetic valves, whether tissue or mechanical, are prone to collecting blood clots. A valve replacement OPERATION is also open heart surgery.

Risk Factors and Preventive Measures

Adults who are over the age of 40 may have had rheumatic FEVER or rheumatic heart disease as children and may be vulnerable to valvular heart disease as a result. Most people under the age of 40 receive antibiotic medications as the standard course of treatment for strep throat, which has greatly reduced the spread of the infection to the heart. Despite these advances, however, nearly 20,000 Americans a year die from valvular heart disease. It remains essential to receive prompt and appropriate treatment for strep infections as well as for early indications of valvular heart disease. People who know or believe they had rheumatic fever in childhood should make sure their doctors are aware of this when having routine medical examinations or receiving treatment for other cardiovascular conditions.

See also CARDIOPULMONARY BYPASS; CARDIOVASCULAR DISEASE PREVENTION; CONGENITAL HEART DISEASE; LIVING WITH CARDIOVASCULAR DISEASE; OBESITY AND CARDIOVASCULAR DISEASE; WEIGHT LOSS AND WEIGHT MANAGEMENT.

varicose veins Distended and distorted veins, typically occurring in the legs. Varicose veins indicate dysfunctional venous valves, which allow BLOOD to backflow or to pool in the VEIN when standing or sitting (VENOUS INSUFFICIENCY). There appears to be a GENETIC PREDISPOSITION for varicose veins, in that they seem to run in families. Varicose veins become more common with increasing age, as the blood vessels lose elasticity and other health conditions become contributing factors. Women are more likely than men to develop varicose veins, though men and women who spend a lot of time standing are at increased risk for varicose veins.

Varicose veins appear enlarged and twisted beneath the skin's surface, most noticeably on the lower legs. For many people, varicose veins are more of a cosmetic than a health concern. Some people experience leg cramps, soreness, and itching. Severe varicose veins result in extensive blood pooling that can cause changes in SKIN color or skin ulcers (venous stasis ulcers) to develop. Most varicose veins respond to conservative treatment such as frequent elevation to relieve the pressure gravity exerts on blood flow. Regular walking

tones and strengthens the muscles of the legs, which then can help to support the veins. The rhythmic movement of the leg muscles during walking also helps push blood through the veins.

Treatment for severe varicose veins may include sclerotherapy, in which the doctor injects a chemical into the varicose vein that causes the vein to SCAR and close. Blood reroutes to other veins, and the varicose vein gradually shrinks and fades to become barely noticeable. LASER SURGERY is effective on smaller varicose veins. For large varicose veins that generate significant PAIN or are causing skin ulcers, the doctor may surgically remove the affected veins in a procedure commonly called vein stripping.

The main complication of varicose veins is DEEP VEIN THROMBOSIS (DVT), in which blood clots form in the pooled or slow-moving blood. The clots cause localized pain and swelling, and if they break free can lodge in the LUNGS, causing PULMONARY EMBOLISM, or in the BRAIN, causing STROKE. Preventive measures include frequent walking, wearing low-heeled shoes (which exercise the muscles in the lower leg), shifting the weight from leg to leg and rocking slightly back and forth when standing is necessary, and resting with the legs elevated.

See also HEMORRHOIDS; PLASTIC SURGERY; TELANGIECTASIS; WALKING FOR FITNESS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

vein A blood vessel that carries BLOOD to the HEART. All veins except the PULMONARY VEINS carry deoxygenated blood; the pulmonary veins return oxygenated blood to the heart from the LUNGS. Because veins lack the muscular structure and contractile capability of arteries, they have valves that keep blood moving only in one direction, toward the heart. The body's largest veins are the superior VENA CAVA and the inferior vena cava, which empty blood into the heart's right atrium.

For further discussion of the veins within the context of cardiovascular structure and function please see the overview section "The Cardiovascular System."

See also ARTERY.

vena cava The body's largest veins, which return deoxygenated BLOOD to the HEART. The superior vena cava brings blood from the upper body and enters the top of the right atrium. The inferior vena cava brings blood from the lower body and enters the bottom of the right atrium. A valve at the juncture of the inferior vena cava and the right atrium, called the eustachian valve, prevents gravity from pulling blood back into the inferior vena cava.

For further discussion of the superior vena cava and the inferior vena cava within the context of cardiovascular structure and function please see the overview section "The Cardiovascular System."

See also AORTA; PULMONARY ARTERIES; PULMONARY VEINS.

venous insufficiency A chronic condition in which the veins cannot adequately return BLOOD to the HEART, usually as a consequence of defective valves that allow blood to leak back and pool in the veins. Some people do not have valves in their veins, a circumstance that is a CONGENITAL ANOMALY. Venous insufficiency primarily affects the veins in the legs, especially the lower legs, and may accompany or contribute to VARICOSE VEINS. Symptoms include edema and characteristic changes in SKIN color and texture (lipodermatosclerosis). Many people who have venous insufficiency experience discomfort, such as burning or itching, and cramping in the lower legs, and may have frequent skin ulcers that are slow to heal. The diagnostic path may include Doppler ULTRASOUND or VENOGRAM to evaluate the flow of blood through the veins.

Treatment is conservative and supportive to the extent possible, including compression stockings to help support the veins and intensify the action of the leg muscles with walking. Frequent walking massages the veins, helping move blood upward toward the heart. Resting with the legs elevated above the level of the heart counters the effect of gravity on returning blood flow. Surgery may become necessary when skin ulcers fail to heal with treatment, or PAIN becomes intense. Surgical options include VEIN ligation (commonly called vein stripping) and vein grafts to reroute blood around severely damaged veins.

See also DEEP VEIN THROMBOSIS (DVT).

venogram A diagnostic procedure to evaluate the flow of blood in the veins, usually in the legs.

The cardiologist may use venogram to diagnose VARICOSE VEINS, VENOUS INSUFFICIENCY, or DEEP VEIN THROMBOSIS (DVT). For venogram, the radiologist injects a small amount of contrast dye into the affected VEIN network and then takes X-rays or fluoroscopy images as the dye moves with the blood through the veins. The venogram shows any structural abnormalities and occlusions. Venogram requires no preparation or recovery. Some people experience a minor burning sensation with injection of the contrast dye. People who are allergic to iodine may have an allergic reaction to the dye.

See also ULTRASOUND; X-RAY.

ventricular assist devices (VADs) Implanted mechanical pumps that aid the native HEART, taking over some of the workload of the ventricles. Several types of VADs are available, each with somewhat different features and functions. A VAD may assist the right or left ventricle, and in some cases both ventricles, as a bridge device while awaiting a donor heart for HEART TRANSPLANTATION or as a permanent device to treat end-stage HEART FAILURE, a therapeutic application sometimes called destination therapy. The VAD sometimes allows the heart to recover sufficiently that the VAD becomes unnecessary and the surgeon can remove it. The OPEN HEART SURGERY to implant the VAD takes between three and eight hours, depending on the person's cardiovascular status and the type of VAD the surgeon is implanting.

Though VADs offer hope of extended survival and improved QUALITY OF LIFE for many people whose heart failure would otherwise be fatal, living with an implanted device requires conscientious and consistent attentiveness. Recipients must take anticoagulant medications and may require other medications, depending on their underlying CARDIOVASCULAR DISEASE (CVD). Ongoing risks include INFECTION, mechanical failure of the VAD, damage to blood cells, bleeding at the implant site, clot formation resulting in STROKE or PULMONARY EMBOLISM, and worsening of cardiovascular status that may require additional therapeutic intervention including surgery. Because the VAD became an approved treatment in the United States only in 2004, doctors do not yet know the long-term benefits and risks of VAD implantation.

See also LIVING WITH CARDIOVASCULAR DISEASE; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; ORGAN TRANSPLANTATION.

ventricular fibrillation Rapid, irregular, ineffective contractions of the heart's ventricles. Ventricular fibrillation quickly becomes fatal without treatment. The HEART cannot pump blood to the LUNGS or to the body when it is in ventricular fibrillation.

Ventricular fibrillation is a life-threatening event that requires emergency medical treatment.

The ELECTROCARDIOGRAM (ECG) provides a definitive diagnosis. Treatment may consist of DEFIBRILLATION (an electrical shock to the heart) or of medications to restore normal rhythm. Ventricular fibrillation typically follows a cardiac crisis such as HEART ATTACK, and despite its lethal potential presents an opportunity for successful resuscitation because the heart still has electrical activity. Ventricular fibrillation may also exist as the deterioration of an ARRHYTHMIA disorder such as ventricular tachycardia (rapid, regular contractions of the ventricles) or WOLFF-PARKINSON-WHITE SYNDROME.

See also ATRIAL FIBRILLATION; CARDIOPULMONARY RESUSCITATION (CPR); PREMATURE VENTRICULAR CONTRACTION (PVC).

Wolff-Parkinson-White syndrome An inherited ARRHYTHMIA disorder in which an extra conduction pathway, called an accessory pathway, exists between the heart's atria and ventricles. The accessory pathway allows the heart's electrical pacing impulse to bypass the normal conductive route, reaching the ventricles before the atria have completed their contraction cycle. While many people who have Wolff-Parkinson-White syndrome never experience any symptoms, some people have episodes of ventricular tachycardia, in which the ventricles contract regularly though very rapidly. Ventricular tachycardia is not very effective in moving BLOOD to the LUNGS and especially through body, resulting in feelings of lightheadedness or episodes of SYNCOPE (brief loss of CONSCIOUSNESS) as the blood supply to the BRAIN becomes diminished.

The ELECTROCARDIOGRAM (ECG) provides the diagnosis, showing the accessory conductive pathway. People who do not have symptoms do not need treatment though should receive regular follow-up evaluation from a cardiologist. When symptoms are present, treatment is necessary and may take the form of medication to regulate the heart's rhythm or RADIOFREQUENCY ABLATION to destroy the extra pathway. Wolff-Parkinson-White syndrome tends to show symptoms in early to middle adulthood. Undetected and untreated Wolff-Parkinson-White syndrome may result in SUDDEN CARDIAC DEATH. With appropriate treatment, most people who have the condition no longer experience symptoms.

See also CARDIAC CYCLE; HEART; LONG QT SYNDROME (LQTS); MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE.

THE BLOOD AND LYMPH

The BLOOD and LYMPH are the cell-bearing fluids that nourish and protect the body. Physician specialists who treat conditions of the blood and lymph are hematologists. This section, "The Blood and Lymph," presents an overview of the structures and functions of the blood and lymph, a discussion of hematologic and lymphatic health and disorders, and entries about the health conditions that can affect the blood and lymph.

Structures of the Blood

BLOOD
PLASMA
BONE MARROW
erythrocytes
  reticulocytes
platelets (thrombocytes)
leukocytes
  lymphocytes:
   B-cells, T-cells
  monocytes
  granulocytes:
   basophils,
   eosinophils, neutrophils
SPLEEN
THYMUS
LYMPH
LYMPH NODES
  cervical nodes
  axillary nodes
  epitrochlear nodes
  inguinal nodes
LYMPH VESSELS
  CISTERNA CHYLI
  THORACIC DUCT
  RIGHT LYMPHATIC DUCT

Functions of the Blood and Lymph

The BLOOD and the LYMPH are the body's vital fluids, sharing responsibility for nourishment, cleansing, IMMUNE RESPONSE, and fluid balance. The blood primarily nourishes the cells, and the lymph cleanses and drains the tissues. The lymph derives from as well as returns to the blood. Though the blood and the lymph are unique fluids that circulate through separate networks, they share some structures that allow leukocytes, notably lymphocytes and granulocytes, to move freely between the blood and the lymph.

The rhythm of life: the blood The adult human body contains about five liters (just under six quarts) of blood that the HEART propels on a continuous circuit through the arteries and veins. Contained within the arteries and veins of the pressurized cardiovascular system, the total blood volume circulates from the heart, through the body, and back to the heart in about a minute. During strenuous activity the blood can pound through six full circuits in a minute, hammering oxygen and GLUCOSE to the cells to fuel their increased energy output.

Though fluid the blood is a living tissue, a mix of cells (45 percent of the blood's composition) suspended in a watery matrix of PLASMA (55 percent of the blood's composition). Plasma, which is about 90 percent water, also carries numerous substances dissolved in it including electrolytes, glucose (sugar), hormones, NUTRIENTS, and proteins such as CLOTTING FACTORS and ALBUMIN. A single drop of blood contains roughly:

- 500 million erythrocytes
- 33.5 million platelets
- 830,500 leukocytes

Blood cell production: the bone marrow The red BONE MARROW, located in cavities within the bones called medullary canals, produces 99 percent of the adult body's blood cells and all of its erythrocytes. This spongy, somewhat gelatinous substance has two structures, the vascular compartments through which blood circulates and the extravascular compartments that contain the BLOOD STEM CELLS. The red bone marrow is extraordinarily active tissue, releasing into circulation 2 to 3 billion erythrocytes, 2 to 3 billion platelets, up to 100 billion granulocytes, and several hundred million monocytes every 24 hours. The BONE

marrow also warehouses minerals it requires for cell synthesis and the bones need for STRENGTH and growth, such as calcium. As well, the bone marrow stores B-cell lymphocytes and plasma cells, leukocytes integral to the body's IMMUNE RESPONSE.

Oxygen transport: erythrocytes The erythrocytes, also called red blood cells (RBCs), pick up oxygen molecules in the LUNGS and carry them to the cells. After delivering the oxygen, the erythrocytes then retrieve carbon dioxide molecules, the waste byproducts of cellular METABOLISM, and cart them back to the lungs for elimination from the body through respiration. This OXYGEN–CARBON DIOXIDE EXCHANGE is the foundation of the body's survival. No cells in the body can survive longer than 10 to 15 minutes (three to five minutes for BRAIN and heart cells) without oxygen.

Erythrocytes acquire their capacity to carry oxygen from the pigmented protein HEMOGLOBIN, which is high in iron. The pigment also gives erythrocytes their red color. The iron hemoglobin contains allows the hemoglobin to bind with the oxygen molecules. A healthy, normal erythrocyte contains about 300 million molecules of hemoglobin; each molecule of hemoglobin can bind with four molecules of oxygen. Iron enters the body from dietary sources. Iron deficiency is the most common cause of ANEMIA, a condition in which the blood cannot meet the body's oxygenation needs.

Erythrocytes are concave on both sides, giving them the FLEXIBILITY to nearly fold in half to squeeze through the narrowest of the body's blood vessels, the arterioles, venules, and capillaries. As well, erythrocytes lack nuclei, the "command" structures common to cells that contain deoxyribonucleic acid (DNA). DNA gives the cell its replication instructions; without it a cell cannot reproduce. The absence of a nucleus further aids the erythrocyte's flexibility, however, which is most important for delivering oxygen deep within the body's tissues.

Because erythrocytes cannot proliferate, the red bone marrow churns out a steady supply of new ones, releasing them into the circulation at a rate of 2 to 3 million per second. Erythrocytes enter the bloodstream in a slightly immature stage, called reticulocytes. They reach full maturity after about 24 hours in circulation and live in the bloodstream for 110 to 120 days, after which the SPLEEN filters them from the blood and breaks them down (hemolyzes) into their component structures. The LIVER further metabolizes the components of hemolyzed erythrocytes, recycling their ingredients for use in synthesizing new erythrocytes as well as to manufacture BILE and other biochemical substances. Macrophages within the liver, migratory monocytes called Kupffer cells, then consume whatever remains of the erythrocytic waste.

Stop the bleeding: platelets The smallest cell elements in the blood, platelets, are encased in protein coatings that become adhesive (sticky) when chemical messengers released at the site of bleeding enter the bloodstream. The chemicals activate PLATELET AGGREGATION, in which platelets swarm to the site of bleeding and stick to each other as well as to the collagen fibers at the site to form a hemostatic plug. This activation also enables platelets to change shape, elongating or contracting as necessary to bridge the gaps among the collagen fibers to form a weblike structure that ensnares other cells and substances. As the coagulation cascade unfolds the plug expands and hardens, eventually forming the clot that halts the bleeding. On the surface of the SKIN, this clot is a scab. Within a blood vessel, it is a thrombus.

Platelets arise from the largest cells in the red bone marrow, megakaryocytes, and actually are fragments of megakaryocytic cytoplasm rather than independent cells. They are irregularly shaped and loosely defined, a structure ideally suited to their purpose. Platelets also lack nuclei and live in the circulation for about 10 days. Roughly a third of the body's total platelet volume resides in the spleen, which releases them into the circulating blood in response to bleeding.

Defend and protect: leukocytes The leukocytes, also called white blood cells (WBCs), are the foundation of the body's IMMUNE RESPONSE. They take one of three forms: LYMPHOCYTE, MONOCYTE, or GRANULOCYTE. Each has specialized functions within the immune response. Lymphocytes attack invading pathogens, and monocytes and granulocytes consume the remains of the pathogenic invaders. Lymphocytes circulate primarily in the lymph. Monocytes circulate in the blood for about 24 hours after the bone marrow releases them and

then migrate into the tissues where they establish themselves as fixed defenders called macrophages. Granulocytes circulate in the blood and in the lymph and also take up residence in the lymph structures and the general body tissues. The three subtypes of granulocytes—basophils, eosinophils, and neutrophils—have specified roles in the body's inflammatory response and are responsible for hypersensitivity reactions and allergies. The bone marrow primarily manufactures leukocytes, with assistance from the lymph tissues and spleen when necessary to meet the body's INFECTION control needs.

Flow with the body: the lymph In contrast to the force of the blood's circulation, the lymph channels through the body at a gentle flow of about 100 milliliters per hour. Gravity and the body's movements (MUSCLE contractions) massage lymph through the lymph vessels that roughly parallel the arteries and veins. The lymph vessels are thin-walled, originating with cul-de-sac structures arising in the epithelial spaces, the lymphatic capillaries, that join increasingly larger channels that carry lymph into the central body and ultimately into the circulating blood.

Slightly more watery than blood (92 percent), lymph carries a suspension of primarily lymphocytes and monocytes as well as dissolved proteins and other substances. Clear and only slightly more viscous than water, lymph drains from the spaces between cells into the lymphatic capillaries, microscopic channels comprised of a single thickness of cells overlapped like backward shingles. This construction encourages fluid to seep under the cells and into the lymph capillaries. The lymph capillaries collect the droplets of lymph, pooling them into microscopic trickles that eventually merge with larger lymphatic vessels—the CISTERNA CHYLI, THORACIC DUCT, and RIGHT LYMPHATIC DUCT—that carry the lymph toward the subclavian veins where it rejoins the bloodstream.

The lymph carries leukocytes, proteins, antibodies, and other materials directly to the cells. While erythrocytes in the blood can carry oxygen molecules into the CAPILLARY BEDS, the capillaries eventually become too narrow even for the flexible erythrocytes to make further passage. So the erythrocytes off-load their oxygen molecules into the lymph, which floats them through the capillary walls and into the interstitial spaces (the space between the cells of the tissues). Lymph flows through the interstitial spaces, bathing the cells, which then withdraw the nutrients, including oxygen and glucose, that they require. Cells also discharge their metabolic wastes into the lymph.

Critical passengers in the lymph are the leukocytes, predominantly neutrophils and lymphocytes. These protective cells vigilantly patrol the interstitial spaces on the alert for invading pathogens. When they detect pathogenic invaders leukocytes secrete chemicals, called CYTOKINES, into the lymph that initiate or activate specific immune responses. Some of these responses recruit additional lymphocytes and granulocytes (notably neutrophils) into circulation both in the lymph and in the blood. As agents of immune response, granulocytes and lymphocytes have the ability to migrate between the blood and the tissues, bolstering the body's defenses as needed.

The lymph also transports pathogens, such as viruses and bacteria, to the lymph nodes where masses of lymphocytes, macrophages (tissue-bound monocytes), and granulocytes wait to dispose of them. The lymph nodes often swell when they are busy fighting infections (LYMPHADENOPATHY) and may themselves become infected (LYMPHADENITIS). The lymph also offers a route of transport for cancer cells that leave the original tumor site. The lymph network can unfortunately carry cancer cells that enter its flow to any location within the body, facilitating METASTASIS (spread of the cancer).

Teaching the concept of self: the thymus The thymus, a loose structure of lymph tissue behind the sternum (breastbone) in the center of the chest, functions somewhat as a prep school for immature T-cells. In the thymus, T-cells learn to distinguish between "self" and "nonself," a fundamental concept of immune function that prevents the IMMUNE SYSTEM from attacking cells that belong to the body. The thymus releases those that learn the lesson, and they migrate into the lymph tissues where they can reside for many years. T-cells that fail to recognize self and nonself do not gain release, and they die without leaving the thymus. In AUTOIMMUNE DISORDERS such as MYASTHENIA GRAVIS and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), it

appears the education of T-cells somehow goes awry, and the thymus releases those that identify certain self cells as nonself. These misguided T cells attack the mistaken self cells as though they were nonself, causing an autoimmune (self-attack) response.

The thymus is most active in childhood, reaching its peak function and size in early ADOLESCENCE. By early adulthood the thymus shrinks to a mere fibrous shadow of its most proliferative self. In the 1940s doctors erroneously drew a correlation between the normally large thymus of childhood and what subsequently became known as SUDDEN INFANT DEATH SYNDROME (SIDS), resulting in "therapeutic" irradiation of the thymus to reduce its size. Unfortunately, this permanently crippled the immune system, an often fatal consequence in a time when antibiotic therapy was in its infancy. Though even today researchers do not fully understand the role of the thymus in adulthood, they know it secretes a number of hormones that appear to have functions related to immune response. THYMECTOMY (surgery to remove the thymus) remains a therapeutic option in very limited circumstances, such as in adults who have myasthenia gravis.

Health and Disorders of the Blood

The blood often is the first location within the body where health conditions manifest, and as well is itself vulnerable to disorders that affect its ability to function. Even conditions that do not directly affect the blood's function show up in the blood, such as DIABETES (elevated blood glucose levels) and ATHEROSCLEROSIS (elevated blood lipids). Diagnostic blood tests, notably the complete blood count (CBC), are part of most clinical evaluations. The numbers, types, and cytologic details of the blood cells provide crucial clues to doctors investigating broad-ranging symptoms such as fatigue, chronic infection, or allergies.

Anemia, an inability of the blood to meet the body's oxygenation needs that affects about 3.5 million people in the United States, results from numerous and varied health circumstances and conditions. SICKLE CELL DISEASE and THALASSEMIA are GENETIC DISORDERS that result in defective erythrocytes. LEUKEMIA, lymphoma, and MULTIPLE MYELOMA are cancers that involve the blood cells and the structures that make them. Inherited deficiencies alter specific aspects of the blood's composition and function, such as HEMOPHILIA, a deficiency of clotting factors that results in excessive bleeding. In many situations treating the underlying health condition eliminates its effect on the blood, such as with many types of anemia. In other cases, such as leukemia, treatment targets the blood or blood-producing organs and structures.

CONDITIONS THAT INVOLVE THE BLOOD AND THE LYMPH

ANEMIA	DISSEMINATED INTRAVASCULAR COAGULATION (DIC)
hemangioma	HEMOCHROMATOSIS
HEMOPHILIA	LEUKEMIA
LEUKOPENIA	LYMPHADENITIS
LYMPHEDEMA	lymphocytopenia
lymphoma	methemoglobinemia
MULTIPLE MYELOMA	MYELODYSPLASIA SYNDROME
MYELOFIBROSIS	NEUTROPENIA
POLYCYTHEMIA VERA	THALASSEMIA
THROMBOCYTHEMIA	THROMBOCYTOPENIA
thrombophilia	thrombosis
VON WILLEBRAND'S DISEASE	

Traditions in Medical History

Though ancient healers understood the importance of blood to health and to life itself, they did not understand the mechanisms of its circulation or production. Doctors did not know these details of physiology until the 17th and 18th centuries, respectively. The great GALEN (129–199), father of Western medicine, pronounced that the liver was the source of the body's blood, constantly producing this vital fluid much as a natural spring produced water, with an equal mix of regularity and mystery. Though centuries later researchers would discover the fragment of truth in this view—the liver does indeed produce the cells of the blood early in fetal development—its fallacy nurtured peculiar medical practices throughout much of modern history. Among the most persistent was that of bloodletting, which remained a mainstay of clinical practice into the 20th century as a treatment for nearly any condition that did not respond to other therapeutic methods. Modern doctors know, of course, that bloodletting drains the body of the cells it needs most to fight infection.

MODERN THERAPEUTIC BLOODLETTING

As was the case with Galen's views on the source of BLOOD, there is also a fragment of validity in the practice of bloodletting. Contemporary physicians use modern variations of this ancient practice to treat several conditions. Therapeutic PHLEBOTOMY withdraws blood to treat HEMOCHROMATOSIS, in which the blood contains too much iron. Therapeutic HEMAPHERESIS selectively extracts components of the blood and returns the remainder to the individual, such as to treat SICKLE CELL DISEASE.

In 1628 British physician William Harvey (1578–1657) refuted Galen's pronouncement with his published evidence of the blood's circulation through a closed network of arteries and veins, establishing the recognition of the blood as a finite composition within the body. Within 20 years physicians began experimenting with BLOOD TRANSFUSION, though what was to become a lifesaving mainstay of medical treatment did not become practical until the early 1900s. Karl Landsteiner (1868–1943), an Austrian-American immunologist, was the first researcher to identify the polysaccharides on the surface of erythrocytes (red blood cells) that were to become known as blood types. The discovery at last explained why one person's blood could harm another person and made possible the therapeutic use of drawing blood from one person for transfusion into another person. Landsteiner won the 1930 Nobel Prize in medicine or physiology for his work, and by the 1950s blood transfusions were standard therapy for a wide range of health conditions.

Transfused blood became a notorious vehicle of death in the early 1980s with the eruption of HIV/AIDS in Western populations. Though scientists had long known of blood's ability to transmit infections such as MALARIA and HEPATITIS, this new VIRUS became a particularly lethal threat for people who relied on chronic blood transfusions to treat health conditions such as hemophilia and sickle cell anemia. It also raised ethical dilemmas in situations of massive trauma in which the only treatment was equally massive transfusions of blood. Thousands of people acquired HIV/AIDS from blood and blood products until reliable screening procedures and testing for the presence of HIV in donor blood became available in the late 1990s.

Breakthrough Research and Treatment Advances

Among the most significant breakthroughs in treatment advances are therapies for cancers of the blood, bone marrow, and lymphatic tissues. Complex CHEMOTHERAPY regimens, bone marrow transplantation, and peripheral blood stem cell (PBSC) transplantation can turn some leukemias from fatal to long-term REMISSION or cure. About 80 percent of children under age 14 who undergo treatment for acute lymphatic leukemia (ALL), for example, experience complete and apparently permanent remission such that doctors are willing to call them cured.

Much current research centers on blood stem cells, with scientists searching for ways to encourage these pluripotent cells to differentiate into cells of types other than blood cells. Peripheral blood stem cells share many of the characteristics of their omnipotent counterparts, embryonic STEM CELLS, including the ability to either replicate themselves or differentiate into specific cell types, and are easy to collect via extraction from BLOOD DONATION or HEMAPHERESIS. Though these efforts have so far met with limited success, they have resulted in new understanding of the complexities that underlie cell differentiation and proliferation in both health and disease.

A

aging, changes in the blood and lymph that occur with The BLOOD undergoes a number of normal changes across the span of the lifetime. Blood cells have life spans ranging from a few hours to decades. The blood continually renews itself, producing millions of erythrocytes and thousands of leukocytes every hour. Blood cell production accelerates to meet unique health needs, such as PREGNANCY or INFECTION.

The LIVER is the first organ in the developing fetus to produce blood cells, primarily erythrocytes, with supplemental production from the SPLEEN and the THYMUS. At about five gestational months the BONE MARROW has developed enough to begin taking over blood cell production and by birth is the primary structure for HEMATOPOIESIS. Through childhood (until about age 16), nearly all the bone marrow is red bone marrow that actively produces blood cells. As the body matures yellow bone marrow, a fibrous structure of connective tissue and fat, gradually replaces the red bone marrow. By adulthood only about 60 percent of the bone marrow is red. This level remains fairly constant until around age 70, when some red bone marrow, primarily in the long bones, again transitions to yellow marrow.

The bone marrow slows ERYTHROCYTE (red blood cell) production in advanced age, putting fewer erythrocytes into the blood's circulation. The reduced erythrocyte volume correspondingly decreases the amount of available HEMOGLOBIN in the blood, which diminishes the amount of oxygen the blood can carry to the cells with each heartbeat. This reduction commonly results in decreased AEROBIC CAPACITY, showing lessened ENDURANCE and longer recovery times with strenuous physical activity, and may cause ANEMIA. The spleen's efficiency at removing old and defective erythrocytes from the circulation declines, an accommodation that is somewhat a double-edged sword. While this slowed hemolytic action allows more erythrocytes to remain in the blood to improve the blood's capacity to carry oxygen, a greater number of those erythrocytes are less effective in this role.

The LYMPH structures and functions also change with age. The lymphatic system becomes active at about age two months when the child's IMMUNE SYSTEM begins to replace the protection from the mother's IMMUNITY. Most of the lymphocytes the lymph tissues produce swarm to the THYMUS, where they will come to maturity. The thymus contains nearly the lifetime complement of immature T-cell lymphocytes (called thymocytes in immaturity) by about age 16, at which point the thymus reaches its peak size and level of function. As the T-cells reach maturity they leave the thymus and migrate to other lymph structures throughout the body where they reside until the immune system needs them. As T-cell maturation winds down the activity of the thymus decreases and the thymus begins to shrink, diminishing by early adulthood to a few clusters of lymph tissue. After adulthood, the body can make only limited additional T-cells. Health conditions that affect T-cells, such as HIV/AIDS, that destroys them can deplete the body's supply of these vital protective cells, depriving the body of its front line immune defense.

With age lymphocyte production also decreases, resulting in fewer circulating lymphocytes and a corresponding reduced resistance to infection. Later in life the spleen diminishes in size, ultimately retreating to about half its size in early adulthood. Its functional capacity decreases as well, resulting in the spleen becoming less efficient at filtering

aged erythrocytes from circulation. The spleen also becomes less effective in fighting infection, reducing the body's resistance.

Other changes in the body that occur with advancing age affect the ability of the LYMPH VESSELS to collect fluid from the tissues and transport it back to the bloodstream. Diminished MUSCLE tone and reduced movement slow the flow of fluids into and through the lymph vessels. Other health conditions such as congestive HEART FAILURE and kidney disease affect the body's ability to move fluids through the blood vessels, creating a backlog. By about age 70, however, the body begins to decrease the total amount of water its tissues retain. This results in less water in the blood and a lower blood volume, somewhat lowering the BLOOD PRESSURE though increasing the risk for blood clots (thrombosis).

See also AGING, CARDIOVASCULAR CHANGES THAT OCCUR WITH; AGING, PULMONARY CHANGES THAT OCCUR WITH; CANCER RISK FACTORS; SENESCENCE.

albumin The most abundant protein in PLASMA. Albumin transports various molecules through the BLOOD and helps sustain the blood's oncotic pressure, keeping fluid from seeping into the tissues. Albumin molecules are larger than the molecules it transports, allowing those substances, such as electrolytes and hormones, to pass through the walls of the blood vessels while the albumin molecules remain within the blood vessels. Albumin is among the numerous plasma proteins the LIVER produces. Albumin is also available as a blood product for transfusion. Blood banks obtain it by separating it, using a cell separator, from donated whole blood or plasma.

The blood of a healthy adult contains 3.5 to 5.0 grams per deciliter (g/dL) of albumin, which makes up about 2 percent of the blood's total volume. A low serum albumin level (hypoalbuminemia, decreased concentration of albumin in the blood) often indicates liver disease such as CIRRHOSIS or kidney disease such as GLOMERULONEPHRITIS. Hypoalbuminemia also occurs with serious BURNS. An elevated albumin level (hyperalbuminemia, increased concentration of albumin in the blood) occurs less commonly and often signals extended DEHYDRATION or DIABETES INSIPIDUS, a disorder of the ADRENAL GLANDS.

See also AGING, CHANGES IN THE BLOOD AND LYMPH THAT OCCUR WITH; BLOOD PRESSURE; BLOOD TRANSFUSION.

anemia A reduced ability of the BLOOD to meet the body's oxygenation needs arising from either a diminished volume of erythrocytes (red blood cells) in the blood or from reduced HEMOGLOBIN content in the erythrocytes. Though the common perception of anemia is that it is itself a health condition, doctors consider anemia an indication of other health conditions. Diagnosis and treatment target those underlying conditions. Anemia affects about 3.5 million people in the United States. Anemia can affect people of any age though is most common among menstruating women and during PREGNANCY.

Causes of Anemia

Anemia may be acute (come on suddenly) or chronic (continue over an extended time). Anemia may also result from medication interactions or ADVERSE REACTIONS, CHEMOTHERAPY, RADIATION THERAPY, and numerous health conditions. In general, anemia results from three circumstances, individually or in combination:

- excessive blood loss drains erythrocytes from the body
- the SPLEEN destroys (hemolyzes) too many erythrocytes
- the BONE MARROW produces too few defective erythrocytes

Blood loss Blood loss, either in large quantity suddenly or through chronic bleeding, has a twofold consequence on the blood's ability to carry oxygen. First, the bleeding reduces the number of erythrocytes in the blood, making fewer erythrocytes and thus less hemoglobin available. Second, old erythrocytes, which the spleen culls from the circulation to dismantle and recycle, are a key source of ingredients such as iron and hemoglobin for the production of new erythrocytes. Traumatic hemorrhage, GASTROINTESTINAL BLEEDING, and heavy menstrual bleeding are among the causes of anemia related to blood loss.

Erythrocyte destruction or deformity One of the spleen's roles is to filter erythrocytes from the blood that are old or defective, a normal process called HEMOLYSIS that maintains an appropriate balance of erythrocytes in the blood. The spleen may inappropriately sequester and destroy healthy erythrocytes, sometimes without apparent reason. SICKLE CELL DISEASE is a complex genetic disorder that results in malformed erythrocytes, causing anemia among other symptoms. In THALASSEMIA, another genetic disorder, erythrocytes are normal but hemoglobin is defective.

Inadequate erythropoiesis Nutritional deficiencies and renal failure are the leading causes of diminished erythropoiesis. The bone marrow requires vitamin B_{12}, iron, and folic acid to manufacture erythrocytes. Pernicious anemia results when the STOMACH fails to produce intrinsic factor, a substance necessary to absorb vitamin B_{12} from ingested foods. When these vital NUTRIENTS are lacking, the bone marrow cannot generate new erythrocytes. Iron deficiency anemia is the most common type of anemia in the United States.

Kidney disease and RENAL FAILURE also affect erythropoiesis because the KIDNEYS secrete ERYTHROPOIETIN (EPO), the HORMONE that stimulates the bone marrow to produce erythrocytes. Bone marrow disorders such as myelofibrosis and MULTIPLE MYELOMA also disturb HEMATOPOIESIS. Aplastic anemia is a life-threatening type of anemia that results when the bone marrow completely shuts down blood cell production.

COMMON CAUSES OF ANEMIA

adverse DRUG reactions	CHEMOTHERAPY
chronic HEPATITIS	CIRRHOSIS
DYSMENORRHEA	environmental toxins
folic acid deficiency	GALLBLADDER DISEASE
GASTROINTESTINAL BLEEDING	HEMOLYSIS
hemorrhage	HIV/AIDS
INFLAMMATORY BOWEL DISEASE (IBD)	iron deficiency
LEUKEMIA	lymphoma
MALABSORPTION syndromes	MULTIPLE MYELOMA
MYELODYSPLASIA SYNDROME	MYELOFIBROSIS
PREGNANCY	RADIATION THERAPY
RENAL FAILURE	SICKLE CELL DISEASE
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	THALASSEMIA
vitamin B_{12} deficiency	

Symptoms and Diagnostic Path

Many people do not have symptoms of anemia but instead find out they have anemia through blood tests conducted for other reasons, such as during ROUTINE MEDICAL EXAMINATION or screening for BLOOD DONATION. When symptoms are present, they are generally the same regardless of the underlying cause and commonly include

- tiredness and fatigue
- breathlessness, especially with physical exercise
- HEADACHE
- chronically cold or tingling hands and feet
- PALPITATIONS or ARRHYTHMIA (irregular or rapid heartbeat)
- irritability
- paleness of the SKIN, nail beds, and gums

Hemolytic anemia may also cause JAUNDICE. Severe anemia can be debilitating, preventing an individual from participating even in everyday activities. Such severe anemias generally result from serious underlying health circumstances. Diagnostic blood tests including complete blood count (CBC), hemoglobin, and hematocrit often provide the initial diagnosis. Further tests might include bone marrow biopsy to determine whether the bone marrow is adequately producing erythrocytes or whether the erythrocytes are normal. The doctor may choose to perform other diagnostic procedures, depending on the findings. Whether or not the anemia causes symptoms, it is important to find its cause.

Treatment Options and Outlook

Most types of anemia are curable or treatable. Treatment targets the underlying cause of the anemia. Supplemental iron, vitamin B_{12}, and folic acid can improve many types of anemia. Pernicious anemia requires lifetime injections of vitamin B_{12}. Aplastic anemia or anemia due to chronic health conditions may require BLOOD TRANSFUSION or BONE MARROW TRANSPLANTATION. Doctors may treat chronic anemia or transient anemia due to cancer treatment with EPO supplementation. Anemia resulting from GENETIC DISORDERS such as sickle cell disease or thalassemia requires ongoing treatment. Successful treatment of the

underlying cause nearly always eliminates the anemia. Most anemias are curable or treatable.

Risk Factors and Preventive Measures

A number of factors can create risk for developing anemia. People who are at greatest risk for anemia are those who

- consume a diet low in iron, folic acid, and vitamin B_{12}, nutrients the bone marrow requires to manufacture erythrocytes
- have gastrointestinal conditions that interfere with nutrient absorption, notably INFLAMMATORY BOWEL DISEASE (IBD), MALABSORPTION disorders, and CELIAC DISEASE
- menstruate or are pregnant
- have chronic health conditions that strain the body's resources, such as AUTOIMMUNE DISORDERS or INFECTION (for example, HEPATITIS or HIV/AIDS)
- have blood disorders; LEUKEMIA, LYMPHOMA, or multiple myeloma; or who are undergoing CHEMOTHERAPY or RADIATION THERAPY for other types of CANCER

People at risk for anemia should have their blood tested regularly and any time they develop symptoms of anemia. Though it is not always possible to prevent anemia, early treatment can minimize the adverse effects of anemia on overall health as well as intervene in the underlying condition at an early stage.

See also DISSEMINATED INTRAVASCULAR COAGULATION (DIC); HEMATOPOIESIS.

apheresis See HEMAPHERESIS.

B

basophil See GRANULOCYTE.

blood The cell-filled fluid that carries vital chemicals and NUTRIENTS via the cardiovascular system to tissues and cells throughout the body. The HEART pumps the blood, sending it under pressure through a closed network of arteries and veins. The blood provides volume within the cardiovascular system, establishing both BLOOD PRESSURE and osmotic pressure (the pressure that keeps fluid within the blood vessels). The blood carries oxygen and nourishment to and collects metabolic wastes from the cells. The blood also serves as the body's primary IMMUNE RESPONSE mechanism, transporting antibodies and specialized cells that defend the body from INFECTION as well as aid in HEALING wounds. The blood's basic composition is about 55 percent PLASMA (liquid) and 45 percent cells. The adult human body contains about five liters, or five and a half quarts, of blood accounting for 8 percent of total body weight.

Plasma

Plasma is 90 percent water. It contains a mix of proteins, electrolytes, hormones, antibodies, minerals, GLUCOSE, and other dissolved substances, forming a solution in which the blood's cells float. The constant churning and movement of the blood as the heart pumps it through the blood vessels keeps the cells and the plasma well mixed. However, in a collected blood sample the cells quickly settle to the bottom, leaving the plasma at the top. The primary proteins in plasma are ALBUMIN, IMMUNOGLOBULIN, and CLOTTING FACTORS. Plasma has a higher concentration of electrolytes (salts) than fluid in the tissues, giving the blood a higher osmotic pressure that draws fluid into the blood rather than allows it to seep from the blood in the CAPILLARY BEDS. Plasma is also essential for COAGULATION (clotting) as it carries both clotting factors and the enzymes that activate them.

Blood Cells

The blood contains three kinds of cells:

- erythrocytes, or red blood cells, which carry oxygen from the LUNGS to every other cell in the body
- leukocytes, or white blood cells, which fight infection and take one of three forms: MONOCYTE, LYMPHOCYTE, or GRANULOCYTE
- platelets, also called thrombocytes, which cause blood to coagulate (clot)

Erythrocytes make up nearly the entire volume of blood cells, while leukocytes and platelets combined make up less than 1 percent. The red BONE MARROW synthesizes (produces) the vast majority of blood cells, a process called HEMATOPOIESIS. Other structures, such as the SPLEEN, can produce limited numbers of blood cells when the body is in crisis. The LIVER and the spleen cleanse damaged, old, and deteriorating blood cells from the blood. The liver breaks erythrocytes into their chemical components, which the body then recycles to synthesize new erythrocytes in the bone marrow.

For further discussion of the blood within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also BLOOD DONATION; BLOOD TRANSFUSION; LYMPH.

blood donation The procedure of withdrawing BLOOD to prepare and use for BLOOD TRANSFUSION. Volunteer donors provide all human blood and

blood products used for transfusions. According to the American Association of Blood Banks, 8 million Americans donate 15 million units of blood each year. Because blood banks separate the majority of donated blood into component blood products, one unit of donated whole blood can meet multiple needs.

The body replaces lost fluid volume (PLASMA) within 24 hours of donation, and erythrocytes (red blood cells) and other blood cells in six to eight weeks. A healthy adult may donate one unit of whole blood every eight weeks. There is no cost for donating blood, and there is very minimal risk. A person cannot contract HEPATITIS, HIV/AIDS, or other infectious diseases through the process of donating blood.

Donor Requirements

In the United States, individual states and blood banks establish regulations and procedures to determine donor eligibility. In general, a prospective donor must

- be 17 years of age or older
- pass a preliminary health screening that identifies potential health risks for the donor or for recipients of the donor's blood
- weigh 100 pounds or more

Health screening questions aim to reveal behaviors or practices that carry a risk for INFECTION with diseases such as hepatitis and HIV/AIDS. Such behaviors include intravenous DRUG use and sex with multiple partners. In 1998, US blood banks also began screening prospective donors for possible exposure to variant Creutzfeldt-Jakob disease (VCJD), the human illness resulting from bovine spongiform encephalopathy ("mad cow" disease). Numerous health conditions may preclude an individual from donating blood; blood banks refer to these exclusions as deferrals.

The Blood Donation Procedure

The total blood donation process takes about 45 minutes to an hour, about 20 minutes of which is the actual blood withdrawal (called PHLEBOTOMY). Once the prospective donor clears the health screening, he or she sits in a reclining chair to be comfortable for the donation process. The technician cleanses the inner arm at the elbow with an antiseptic and puts a tourniquet briefly around the upper arm to cause the veins to engorge. The technician then inserts a sterile needle, connected to collection tubing and bag, into one of the veins and releases the tourniquet.

The technician may ask the person to periodically squeeze an object to help move blood through the VEIN during collection. After blood fills the collection bag (one unit), the technician withdraws the needle and places pressure over the puncture site for several minutes to suppress any bleeding, then applies a bandage that should stay in place for two to four hours. The person moves to a resting area, usually to have a drink of juice or water and a snack, then may leave when he or she feels comfortable. The risks associated with donating blood are very minor and may include bleeding, bruising, or discomfort at the needle insertion site.

Donor Blood Distribution and Use

Most donated blood goes to centralized blood banks for distribution to hospitals, which administer it to anyone who needs it. Two exceptions are

- autologous donation (BLOOD AUTODONATION), in which an individual donates blood for his or her own transfusion such as for a planned major surgery
- directed donation, in which an individual asks that others donate blood on his or her behalf and specified use, such as following a major trauma or unanticipated major surgery

Blood banks generally cannot use blood not used for self-transfusion (autologous donation) or not administered to the intended recipient (directed donation) for general transfusions and must instead throw it away. Some blood banks screen and process autologous donations differently from general donations, making autologous donations unacceptable for general use. Other blood banks handle autologous and general donations the same and have procedures for donors to authorize, at the time of donation, other use of their blood under such circumstances to avoid unnecessary waste of such a valuable resource. Though blood banks screen and process directed

donations the same as general donations, many health experts are concerned that donors may not be forthcoming during the health screening process, raising the risk for the blood to carry pathogens. The tests blood banks run on each unit of donated blood may not detect the presence of certain infections, making accurate health screening essential.

See also BONE MARROW DONATION; CREUTZFELDT-JAKOB DISEASE (CJD); HEMOCHROMATOSIS; HEMAPHERESIS.

blood stem cells The parent cells from which all BLOOD cells arise. Blood stem cells are pluripotent or undifferentiated, which means they have the ability to become any of the three types of blood cells (erythrocytes, leukocytes, or platelets). Intricate biochemical interactions determine how the blood stem cell will differentiate (become a specific type of blood cell). Blood stem cells reside primarily in the BONE MARROW and the LYMPH tissues though some circulate in the blood.

Blood stem cell transplantation, with harvesting through BONE MARROW DONATION and peripheral blood stem cell (PBSC) donation, has become a cornerstone of treatment for cancers involving the bone marrow and blood, notably leukemias and lymphomas. Researchers are exploring ways to use blood stem cells in other ways. Unlike embryonic stem cells, which are omnipotent (can differentiate into any kind of cell), blood stem cells have limited capability to differentiate only into the various types of blood cells. However, the abundance and ease of collection of blood stem cells, which can be extracted from the blood, gives researchers hope that they may discover methods to manipulate blood stem cell differentiation to give rise to other kinds of cells.

See also BONE MARROW TRANSPLANTATION; CELL STRUCTURE AND FUNCTION; HEMATOPOIESIS.

blood transfusion A therapeutic procedure to administer BLOOD or blood products. Blood transfusions may be autologous (self-donated), when the timing of the need for blood permits planning, or allogeneic (volunteer donor). The transfusion of blood or blood products takes place intravenously, through a sterile needle inserted into a VEIN. Receiving a transfusion may take 10 to 20 minutes, depending on the blood product, condition of the recipient's veins, and the urgency with which the person needs the blood product. Frozen blood products are thawed, and most blood products are brought to body temperature, before administration.

BLOOD RECLAMATION DURING SURGERY

Many hospitals use BLOOD reclamation, also called blood collection, procedures to collect, cleanse, and return to the person during the OPERATION blood lost during a major surgery such as orthopedic, transplant, or OPEN HEART SURGERY. This practice reduces the need for blood transfusions.

Blood Type Compatibility

Though physicians attempted blood transfusions as early as the 17th century, many hazards and failures accompanied the procedure until researchers discovered blood types in the early 1900s. The techniques to allow consistent detection of BLOOD TYPE, called type and cross-match, finally became available in the 1950s. Doctors then were able to routinely match the blood type and rhesus (Rh) factor of donors to recipients and blood transfusions became a standard element of medical care. Transfusion of whole blood and cell-containing blood products such as red blood cells (erythrocytes) requires blood type compatibility between donor and recipient; transfusion of other blood products such as PLASMA, ALBUMIN, and CLOTTING FACTORS does not.

BLOOD PRODUCTS FOR TRANSFUSION

whole BLOOD	packed red blood cells
PLASMA	ALBUMIN
clotting factor VII	clotting factor IX
platelets	cryoprecipitated antihemophilic factor (AHF)
fibrinogen	anti-inhibitor coagulation complex (AICC)
antithrombin III	alpha 1-proteinase inhibitor
IMMUNOGLOBULIN	
Rh immunoglobulin	
granulocytes	

Transfusion Reaction

Blood type incompatibility, though uncommon in transfusion, can lead to reactions spanning the spectrum from mild to fatal. Comprehensive type

and cross-match procedures of donor and recipient blood types prevent most blood incompatibility, though situations of extreme urgency (in which thorough type and cross-match is not possible) and occasionally human error result in incidents in which a blood transfusion recipient receives blood that is incompatible with his or her blood type. As well, blood may contain antigens that conventional type and cross-match procedures do not detect. People who have health conditions (such as SICKLE CELL DISEASE, THROMBOCYTHEMIA, and HEMOPHILIA) that require frequent or numerous transfusions often develop antibodies to other antigens commonly present in blood, increasing their risk for transfusion reaction.

Symptoms of transfusion reaction develop within 24 hours of receiving blood, though often begin during the transfusion, and may include

- FEVER
- chills
- URTICARIA (hives)
- PAIN in the lower back
- generalized physical discomfort

Mild transfusion reactions resolve with minimal medical intervention, such as medications to relieve fever and discomfort. Moderate to severe transfusion reaction may require CORTICOSTEROID MEDICATIONS to thwart the body's IMMUNE RESPONSE. Rarely, transfusion reaction can progress to thromboembolism that blocks the flow of blood through key arteries, including in the LUNGS to cause PULMONARY EMBOLISM, and cardiovascular SHOCK. Such severe complications are potentially fatal and require emergency medical treatment for the specific complications.

Transfusion-Transmitted Infections

Despite comprehensive screening tests and procedures, blood-borne infections remain a risk of blood transfusions. Screening can detect pathogens and antibodies that indicate the presence of infection for a number of blood-borne health conditions including HIV/AIDS, HEPATITIS (HVA, HVB, HVC), and SYPHILIS. Screening tests are only marginally successful at detecting other infections such as CYTOMEGALOVIRUS (CMV) and human T-lymphotropic virus (HTLV). Other pathogens are able to escape detection, notably those responsible for west Nile virus, MALARIA, and CREUTZFELDT-JAKOB DISEASE (CJD) as well as various BACTERIA.

Nearly all infections involve a time gap, the infection's INCUBATION PERIOD, during which the INFECTION is present in the blood though has not yet caused symptoms or antibodies. The risk for transfusion-transmitted infections is highest for blood donated during this phase of infection. Some blood banks are using a technology called nucleic acid testing (NAT), also called nucleic acid amplification testing, that can detect a virus's genetic material in the blood. This allows detection of the infection before the IMMUNE SYSTEM develops antibodies, shortening the window of time during which the PATHOGEN is present and infectious but undetectable.

INFECTIONS THAT BLOOD PRODUCT TRANSFUSIONS CAN TRANSMIT

BABESIOSIS	CREUTZFELDT-JAKOB DISEASE (CJD)
CYTOMEGALOVIRUS (CMV)	HEPATITIS A (HVA)
hepatitis B (HVB)	hepatitis C (HVC)
HIV/AIDS	human T-lymphotropic virus 1 (HTLV-1)
MALARIA	variant CJD (VCJD)
SYPHILIS	
west Nile virus	

See also BLOOD AUTODONATION; BLOOD DONATION; BONE MARROW DONATION; BONE MARROW TRANSFUSION; DISSEMINATED INTRAVASCULAR COAGULATION (DIC); HEMAPHERESIS; STEM CELL.

blood type The pattern of specialized proteins, called agglutinogens or antigens, present on the surface of the red BLOOD cells (erythrocytes). The presence of antigens on the erythrocytes causes the IMMUNE SYSTEM to create oppositional antibodies, which will attack cells bearing the opposing antigens. Antigens and corresponding antibodies begin to develop shortly following birth. The discovery of blood types in the early 1900s made successful BLOOD TRANSFUSION possible, earning researcher Karl Landsteiner (1868–1943) the 1930 Nobel Prize in medicine or physiology. Landsteiner was also among the group of scientists who discovered the rhesus (Rh) factor, another red blood cell antigen, in the 1940s.

ABO Blood Types

There are four blood types: A, B, AB, and O. Each designates the presence or absence of specific blood antigens and antibodies. Each type causes an immune reaction to blood from its opposite type. The exception is type O blood, which has no antigens on its cell surfaces. Type AB blood has antigens A and B on its cell surfaces. Doctors sometimes refer to people who have type O blood as universal donors because people of any blood type can receive emergency transfusions of type O blood (preferably as packed red blood cells containing little of the antibody-carrying PLASMA), and people who have type AB blood as universal recipients because they can receive blood of any type in emergency transfusions.

ABO BLOOD TYPES

Blood Type	Antigens on Erythrocytes	Antibodies in Plasma
A	A	anti-B
B	B	anti-A
AB	A and B	none
O	none	anti-A and anti-B

Rh Blood Types

Blood typing further incorporates tests for the presence or absence of a group of antigens known collectively as the rhesus (Rh) factor. The name derives from the rhesus monkey, the animal in which researchers first isolated the antigens. When the antigens are present on the erythrocytes the designation is Rh positive (Rh+); when the antigens are not present the designation is Rh negative (Rh–). Less than 15 percent of the American population has Rh– blood. Though collectively there are more than 40 identified antigens in the Rh blood type system, nearly all antibody response arises from Rh-D antigens. Most blood type classifications represent the ABO type and Rh status together, as in AB+ or O–.

An immune response occurs when Rh+ and Rh– blood mingle, irrespective of the ABO blood type. The health risk is to the individual whose blood is Rh–. Rh incompatibility is a serious threat to the life of an unborn child and can manifest when a mother who is Rh– conceives a child who is Rh+. The first commingling of Rh-incompatible blood typically does not result in adverse effects because the mother's Rh– blood does not yet contain antibodies against the fetus's Rh+ blood, but the first exposure to Rh+ blood activates ANTIBODY production in the mother. The first child in an Rh-incompatible pregnancy typically is born without complications; however, subsequent pregnancies result in the mother's body producing massive Rh+ antibodies that cross the PLACENTA and destroy the fetus's Rh+ erythrocytes. This condition, called hemolytic disease of the newborn (HDN) or erythroblastosis fetalis, often kills the unborn child.

The standard of PRENATAL CARE in the United States includes blood tests to determine maternal Rh status, with an injection of Rh IMMUNOGLOBULIN to prevent antibody formation in women who have Rh– blood. Rh incompatibility also can cause transfusion reaction when a person who has Rh– blood receives Rh+ blood. Such transfusion reactions can cause serious ANEMIA and cell agglutination (clumping) that can result in death.

Distribution of Blood Types

The most common blood type among Americans is O+ (38 percent); the least common is AB– (1 percent). Genes determine blood type (ABO as well as Rh). Before the advent of DNA sequencing and HUMAN LEUKOCYTE ANTIGENS (HLAS) typing, blood type was the basis of paternity testing. There are enough variations in blood type INHERITANCE PATTERNS, however, to make blood type less than 100 percent reliable for determining parentage, and blood type is no longer legal proof of parentage in the United States.

PERCENTAGES OF BLOOD TYPES AMONG AMERICANS

type O+	38 percent
type A+	34 percent
type B+	9 percent
type O–	7 percent
type A–	6 percent
type AB+	3 percent
type B–	2 percent
type AB–	1 percent

Source: American Association of Blood Banks, 2005

See also BLOOD AUTODONATION; BLOOD DONATION.

bone marrow The semigelatinous tissue within the center of the BONE. Though its presence is imperceptible in health, the bone marrow is the

foundation of the BLOOD and its circulation and plays a fundamental role in immune function. Red bone marrow is the primary source of new blood cells and is most abundant within the sternum, ribs, vertebrae, and pelvis in an adult. In childhood the bones of the skull and face, and the long bones of the arms and legs, also contain red bone marrow. As the body matures the red bone marrow in these sites transitions to yellow bone marrow, which contains mostly connective tissue and fat. The healthy adult has less than half as much red bone marrow as blood.

About 99 percent of the red bone marrow's output is erythrocytes; erythropoiesis is the process of producing erythrocytes. The red bone marrow also produces platelets (clotting cells) and granulocytes, a type of LEUKOCYTE (white blood cell). The cells that make up the bone marrow are BLOOD STEM CELLS, which continuously replicate to replenish the bone marrow and differentiate into three parent lines, or precursors, that produce blood cells. The parent lines are

- erythroblasts, which produce erythrocytes
- megakaryoblasts, which produce platelets
- myeloblasts, which produce neutrophils, basophils, and eosinophils (the three subtypes of granulocytes)

The red bone marrow also warehouses plasma cells, which are integral to immune function (not related to the PLASMA that forms the fluid base of blood). The red bone marrow is the location where B-cell lymphocytes, which migrate to the marrow from the LYMPH tissues that produce them, come to maturity. Yellow bone marrow produces a few leukocytes in adulthood though primarily functions as a reserve resource for new blood cell production when the red bone marrow cannot meet the body's needs.

DISORDERS THAT AFFECT THE BONE MARROW

ANEMIA	LEUKEMIA
LEUKOPENIA	metastatic CANCER
MULTIPLE MYELOMA	MYELODYSPLASIA SYNDROME
MYELOFIBROSIS	NEUTROPENIA
POLYCYTHEMIA VERA	radiation toxicity
THROMBOCYTHEMIA	THROMBOCYTOPENIA

For further discussion of the bone marrow within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also CELL STRUCTURE AND FUNCTION; ERYTHROPOIETIN (EPO); HEMATOPOIESIS; SPLEEN.

bone marrow donation The withdrawal of BONE MARROW from a donor for use as a BONE MARROW TRANSPLANTATION or to harvest BLOOD STEM CELLS, usually as treatments for LEUKEMIA, lymphoma, some other cancers, and severe forms of ANEMIA. BONE marrow donation may be autologous (donated for reimplantation into the donor) or allogeneic (donated for another person to receive as a bone marrow transplantation).

Bone marrow donation is a surgical procedure performed in an operating room under general ANESTHESIA. The physician extracts donor bone marrow, which is a thick liquid, using a syringe and a large needle that can pierce the bone. The most common donor site is the iliac crest (hip bone). A single bone marrow donation typically harvests about 1 quart (less than a liter) of red bone marrow mixed with BLOOD. The donor's body replaces the extracted marrow in about four to six weeks. The risks of bone marrow donation are slight. They include postoperative bleeding and INFECTION. The withdrawal site is typically uncomfortable for a few days after the donation.

There is no cost to the donor for the bone marrow donation procedure and care related to it unless the donor is also to be the recipient (autologous donation). Prospective donors register with a bone marrow donor program, which uses blood samples to identify tissue types. The program contacts the prospective donor when there is a need for marrow of his or her tissue type. Unlike blood donated for transfusions, bone marrow cannot be stored.

A less invasive type of donation that appears to achieve the same result is peripheral blood stem cell (PBSC) collection, done through a procedure called HEMAPHERESIS (also called apheresis). Hemapheresis is similar to BLOOD DONATION, in which an intravenous (IV) line withdraws the donor's blood. The blood goes into a blood separator that extracts the blood stem cells and returns the remainder of the blood to the donor via a second

IV line in a different VEIN. Before PBSC the person may receive injections of a medication to stimulate the bone marrow to increase its production of blood stem cells, to increase their numbers in the blood. The blood yields a lower volume of blood stem cells than does bone marrow.

See also BLOOD TRANSFUSION.

bone marrow transplantation A therapeutic procedure to replace the BLOOD STEM CELLS, the functional component of BONE MARROW, with healthy donor BLOOD stem cells. Typically the preparation process for the BONE marrow removes T-cells and sometimes other leukocytes (white blood cells) to lower the likelihood of ANTIGEN response in the recipient. Common reasons for bone marrow transplantation include

- some types of LEUKEMIA
- some types of lymphoma
- some other cancers that have not responded to first line treatments
- severe aplastic ANEMIA

Bone marrow transplantation is a complex and fairly high-risk procedure because the recipient's native bone marrow must first be destroyed, which wipes out the body's IMMUNE RESPONSE capability. Doctors accomplish this through high-DOSE CHEMOTHERAPY or RADIATION THERAPY. After this preparation, the recipient must remain in protective isolation in the hospital to limit exposure to pathogens such as viruses and BACTERIA.

The transplant recipient receives the bone marrow blood stem cells, tissue-matched for compatibility between donor and recipient, via infusion into an intravenous line, much like receiving a BLOOD TRANSFUSION. The transplanted blood stem cells migrate to the bone marrow where they establish themselves (a process called engraftment). The migration and engraftment takes about three to four weeks, after which the transplanted blood stem cells begin producing new blood cells. The immune functions of the bone marrow and blood cells begins to return in about six months, though is not complete for as long as two years. During this replenishment stage the person remains especially vulnerable to INFECTION. As well, some people take IMMUNOSUPPRESSIVE THERAPY to reduce the risk for rejecting the transplanted blood stem cells. Immunosuppression further limits the immune response.

The primary risks of allogeneic (volunteer donor) bone marrow transplantation are infection and, with allogeneic donation, rejection of the transplanted blood stem cells. There is no risk for rejection with autologous donation. Infection, however, can erupt at any time and has high risk for serious or fatal consequences for as long as the person's immune response cannot provide protection. Early intervention with ANTIBIOTIC MEDICATIONS can head off or reduce the severity of many bacterial infections. Frequent blood tests monitor the return of healthy blood cells to the circulation. The success of bone marrow transplantation is highly variable and depends on numerous factors, including the kind of cancer and the general health of the person aside from the cancer. When successful, bone marrow transplantation can put the cancer into extended and sometimes permanent REMISSION.

See also BONE MARROW DONATION; CANCER TREATMENT OPTIONS AND DECISIONS; GRAFT VS. HOST DISEASE; ORGAN TRANSPLANTATION.

C

Christmas disease See HEMOPHILIA.

cisterna chyli A saclike structure of the lymphatic system, located behind the STOMACH, that collects LYMPH draining from the abdomen, notably the gastrointestinal region, and the lower body. The cisterna chyli empties into the THORACIC DUCT.

For further discussion of the cisterna chyli within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also LYMPHEDEMA; LYMPH VESSELS; RIGHT LYMPHATIC DUCT.

clotting factors Proteins in the BLOOD that are essential for COAGULATION. Clotting factors circulate in the blood as inert proteins until the coagulation cascade initiates their conversion into participants

CLOTTING FACTORS

Clotting Factor	Common Name	Function
antithrombin	antithrombin III, antithrombin III, COAGULATION inhibitor, AT-III	regulates thrombin, factor IX, factor X, factor XI, and factor XII to inhibit the coagulation cascade
factor I	fibrinogen	forms fibrin clot after activation by thrombin in the final common pathway
factor II	prothrombin	together with factor Xa prothrombinase converts prothrombin into active thrombin, which in turn helps PLATELET AGGREGATION
factor III	tissue factor	initiates extrinsic coagulation cascade following vascular injury cofactor with factors VII, VIII, and IX in activating factor X cofactor in activation of factor VII
factor IV	calcium	required at several points in the coagulation cascade
factor V	proaccelerin or accelerator globulin	necessary to stop coagulation cascade at the end
factor VI	accelerin, factor Va	activated form of factor V together with factor X converts prothrombin to thrombin in the final common pathway

Clotting Factor	Common Name	Function
factor VII	serum prothrombin conversion accelerator (SPCA) or cothromboplastin	activates factor X when calcium and factor III (tissue factor) are present
factor VIII	antihemophilic factor A	activates platelet aggregation and adhesion cofactor with factor IX in activating factor X
factor IX	Christmas factor, antihemophilic factor B, or plasma thromboplastin component (PTC)	cofactor with factor VIII in activating factor X (vitamin K-dependent)
factor X	Stuart factor or Stuart-Prower factor	activated by complex of tenase (factors VII and IX), factor VII, and calcium to enable platelet aggregation Initiates conversion of factor II (prothrombin) to thrombin
factor XI	plasma thromboplastin antecedent (PTA)	in the intrinsic pathway, activates factor IX when calcium is present
factor XII	Hageman factor	activates factor XI, thereby starting the intrinsic pathway binds to exposed collagen at site of intravascular injury
factor XIII	fibrin stabilizing factor (FSF), fibrinoligase, fibrinase, plasma transglutaminase, Laki-Lorand factor, LL factor, LLF, or protransglutaminase	cross-links and stabilizes fibrin clot after activation by thrombin needs calcium as cofactor
high molecular weight kininogen (HMWK)	contact activation factor, Fitzgerald factor, Flaujeac factor, Williams-Fitzgerald-Flaujeac factor, or Williams factor	activates factor XII early in the intrinsic pathway
prekallikrein	Fletcher factor or prokallikrein	activates factor XII at very beginning of the intrinsic pathway
protein C	anticoagulant protein C	limits functions of factor V and factor VIII with cofactor protein S, inhibits thrombin to block fibrin clot formation
protein S	anticoagulant cofactor protein S	limits functions of factor V and factor VIII as cofactor for protein C, inhibits thrombin to block fibrin clot formation
thrombomodulin	fetomodulin	cell surface receptor that binds excess thrombin, thus inhibiting dangerous clot formation

in blood clotting. Clotting factors interact with each other as well as other enzymes in the blood, notably fibrin and thrombin, to form blood clots. Deficiencies of specific clotting factors cause coagulation disorders such as HEMOPHILIA (excessive bleeding) and thrombophilia (excessive clot formation). The LIVER produces clotting factors I (fibrinogen), II (prothrombin), V (proaccelerin), VII (cothromboplastin), IX (PLASMA thromboplastin), and X (Stuart-Prower factor).

See also ANTICOAGULANT THERAPY; ASPIRIN THERAPY.

coagulation The process, also called the coagulation cascade, through which the BLOOD forms clots. The cells responsible for forming clots are platelets, which interact with each other, collagen, proteins, and other substances in the blood. Specialized proteins in the blood, called CLOTTING FACTORS, activate in cascades, with one activation leading to another in sequence. Coagulation begins with one of two sequences of cascading events: either an extrinsic or an intrinsic trigger sets off a different cascade. Each cascade culminates in clot formation. Current research suggests that coagulation cascades unfold at different paces and with differing thresholds of activation according to the type of tissue or the organ structure involved. This way, the body manages the coagulation process appropriately to the situation.

Coagulation is a beneficial event when it stops bleeding and can become a hazard to health when it occurs inside blood vessels. Insufficient clotting allows extended bleeding, and excessive clotting can result in HEART ATTACK, STROKE, PULMONARY EMBOLISM, and DEEP VEIN THROMBOSIS (DVT). Though the coagulation process includes several inherent checks and balances that ordinarily strike a balance between beneficial and harmful clotting, problems with coagulation can occur and can be life-threatening.

Coagulation disorders occur when certain clotting factors are missing (such as in HEMOPHILIA), which results in excessive bleeding, or when there is an abundance of platelets in the blood (such as in THROMBOCYTHEMIA), resulting in excessive clotting. LIVER disease such as CIRRHOSIS or severe HEPATITIS affects the liver's ability to produce clotting factors—especially factors II, VII, and X—and to metabolize VITAMIN K (which participates in converting a number of clotting factors from inactive to active states), impairing coagulation.

Extrinsic coagulation cascade Any breach in a blood vessel, such as a cut (even microscopic), causes blood to come into contact with tissue factor (clotting factor III), a protein on the surface of epithelial cells (the cells of the SKIN, mucous membranes, and lining of the blood vessels). Tissue factor initiates the extrinsic coagulation cascade, activating the release and interactions of thromboplastin, clotting factor VII, and calcium ions to culminate in the production of clotting factor X.

Intrinsic coagulation cascade Internal clot formation occurs without a breach when the blood comes into contact with a foreign substance in the blood such as an ATHEROSCLEROTIC PLAQUE that activates the body's INFLAMMATION response, resulting in the formation of collagen. Collagen's presence initiates the release of kallikrein and high molecular weight kininogen (HMWK), two substances that activate clotting factor XII. The continued interaction among these substances draws clotting factor XI and clotting factor IX into the process, culminating in the production of clotting factor X.

Clot formation PLATELET AGGREGATION and clot formation begin at the intermediate level of either cascade, when clotting factor X initiates the conversion of clotting factor II (prothrombin) into the enzyme thrombin. Thrombin in turn converts clotting factor I (fibrinogen) to fibrin, a protein that interlaces with collagen (formed by the IMMUNE SYSTEM's inflammation response) to form a clot. The clot attracts additional platelets, extending the coagulation process until the protein thrombomodulin activates protein C, beginning the coagulation inhibition cascade that brings coagulation to a halt.

See also ANTICOAGULATION THERAPY; ASPIRIN THERAPY; CORONARY ARTERY DISEASE (CAD); C-REACTIVE PROTEIN; HEALING; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; SCAR.

D–G

disseminated intravascular coagulation (DIC) A secondary COAGULATION disorder arising from an imbalance among the CLOTTING FACTORS in the BLOOD. DIC occurs as a result of a significant underlying health condition such as HIV/AIDS, overwhelming infections, or CANCER, and as a serious complication in PREGNANCY. DIC is a symptom rather than a condition. Indications of its presence include

- PETECHIAE (pinpoint hemorrhages), especially on the roof of the MOUTH (soft palate) and the lower legs
- ECCHYMOSIS (easy bruising)
- hemorrhage (easy bleeding)
- thrombosis (clot formations in the blood vessels, typically the veins)

The diagnostic path includes blood tests, especially fibrinogen and fibrin split products. Treatment for DIC targets the underlying cause, though may include measures such as BLOOD TRANSFUSION to arrest hemorrhaging or ANTICOAGULATION THERAPY when the condition manifests as thrombosis. The outlook, like the treatment, depends on the underlying cause.

See also PLATELET.

eosinophil See GRANULOCYTE.

erythrocyte A red BLOOD cell (RBC). The primary function of erythrocytes is to carry oxygen from the LUNGS to the cells of tissues throughout the body and return carbon dioxide, a metabolic waste, to the lungs for removal from the body. Erythrocytes contain iron and HEMOGLOBIN, a pigmented protein that gives them their red color. Hemoglobin is the substance to which oxygen and carbon dioxide molecules bind for transport through the bloodstream. Erythrocytes account for 99 percent of the blood cells the blood carries.

Erythrocytes lack nuclei, which means they cannot proliferate (reproduce). They have a lifespan of about 120 days. The BONE MARROW thus must continuously produce erythrocytes, which it does at the rate of about 2 million per minute. The SPLEEN and the LIVER filter aging, deteriorating, and defective erythrocytes from the blood circulation. Men have a somewhat higher percentage of erythrocytes in their blood, about 47 percent, than women, who have about 42 percent, primarily because women lose blood each month with MENSTRUATION. The number of erythrocytes in both men and women begins to decline after age 70 because erythropoiesis slows as a natural aspect of aging.

For further discussion of erythrocytes within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also HEMATOPOIESIS; OXYGEN–CARBON DIOXIDE EXCHANGE.

erythropoiesis See HEMATOPOIESIS.

erythropoietin (EPO) A HORMONE the KIDNEYS produce that stimulates the BONE MARROW to increase red BLOOD cell production. EPO is a protein structure called a CYTOKINE. Specialized cells in the renal cortex, called peritubular fibroblasts, respond to the amount of oxygen in the blood as it passes through the kidney. When the oxygen saturation of the blood is low (HYPOXIA), the peritubular fibroblasts increase EPO production. Normally the bone marrow releases about two million

erythrocytes into circulation every minute. The EPO stimulates the bone marrow to release higher numbers of erythrocytes into the blood circulation, which boosts the amount of HEMOGLOBIN and increases the blood's capacity to carry oxygen.

EPO production falters in serious kidney disease, resulting in ANEMIA. Medications that diminish kidney function may have similar effects. The liver and perhaps other sites in the body also produce small amounts of EPO, though not enough to meet the body's needs when the kidneys fail. Some people experience fluctuations in EPO production, both increases and decreases, after KIDNEY TRANSPLANTATION.

During the 1980s researchers identified and sequenced the GENE responsible for EPO, allowing the synthesis of recombinant erythropoietin in the laboratory. Administered by injection, this form of EPO, epoetin alpha (Procrit, Epogen), can supplement or replace endogenous EPO to stimulate the bone marrow when kidney production falls off or other circumstances cause rapid ERYTHROCYTE depletion and corresponding anemia. Potential side effects of EPO supplementation include increased BLOOD PRESSURE (HYPERTENSION) especially when the cause of anemia is RENAL FAILURE, and thrombosis (the formation of blood clots within the blood vessels) resulting from the increased percentage of erythrocytes in the blood.

See also BLOOD DOPING; CYTOKINES; HEMATOPOIESIS; MULTIPLE MYELOMA.

granulocyte A type of LEUKOCYTE (white BLOOD cell) so named because its cytoplasm contains granules. The granules, called lysosomes in neutrophils, contain enzymes that digest proteins and carbohydrates, the basic components of cellular structures. Granulocytes are primarily phagocytic; their responsibility is to consume pathogens that lymphocytes and other leukocytes neutralize as part of the body's IMMUNE RESPONSE. Pathologists refer to granulocytes as polymorphonuclear (PMN) because the nucleus of a granulocyte contains multiple lobes. Granulocytes have a short life span in the circulation, typically six to eight hours. After this time some of them migrate into the tissues and continue to function as phagocytes. The liver filters from circulation those that do not migrate and its phagocytic cells, the Kupffer cells, consume them. There are three types of granulocytes, named for the kinds of tissue dyes they accept to emphasize their structures for microscopic examination: basophils, eosinophils, and neutrophils.

Basophils A basophil accepts a base dye such as methylene blue, accounting for its name, which means "base-loving." Basophils respond to the various chemicals injured cells and pathogens release, among them HISTAMINE, serotonin, CYTOKINES, LEUKOTRIENES, and PROSTAGLANDINS. Basophils themselves also release these chemicals, which serves to further incite an inflammatory response as well as summon more leukocytes into action. Basophils filled with HISTAMINE granules are primarily responsible for HYPERSENSITIVITY REACTION and ALLERGY responses. They are abundant in the bronchial tissues during ASTHMA attacks, for example, and in the tissues surrounding an insect bite or sting.

Eosinophils The eosinophil ("eosin-loving") accepts a tissue dye called eosin for examination under the light microscope. Eosinophils, containing enzymes to digest bacteria and other pathogens, also have roles in histamine release (such as in hypersensitivity reactions and asthma) and inflammatory response. Parasitic infections, atopic DERMATITIS, non-Hodgkin's LYMPHOMA, and OVARIAN CANCER are among the conditions that can cause elevated eosinophil levels. Medication reactions, notably with beta blockers and CORTICOSTEROID MEDICATIONS, are among the causes of lowered eosinophil levels. An eosinophil normally circulates about eight hours in the blood and then migrates into the tissues.

Neutrophils The neutrophil ("neutral-loving") stains neutrally for microscopic examination. It is the most abundant type of leukocyte in the blood, making up about 70 percent of the white blood cells in circulation. Neutrophils are the IMMUNE SYSTEM's infantry, maintaining a strong defensive presence in the blood and swarming to attack invading pathogens. Neutrophils that die in the line of duty release toxic chemicals to continue their protective actions. Neutrophils are integral to the body's inflammatory response and are often to blame for autoimmune attacks such as those that occur with RHEUMATOID ARTHRITIS and INFLAMMATORY BOWEL DISEASE (IBD). Numerous health conditions can lower the number of neutrophils in the blood circulation

including infections, serious vitamin B deficiency, RADIATION THERAPY, CHEMOTHERAPY, and cancers such as LEUKEMIA and lymphoma. Some medications, notably antibiotics and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), can also decrease the neutrophil level raising the risk for INFECTION.

For further discussion of granulocytes within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also CELL STRUCTURE AND FUNCTION; LYMPHOCYTE; MONOCYTE.

H

hematopoiesis The process through which the body generates new BLOOD cells. In the adult, the red BONE MARROW and the LYMPH tissues (primarily the lymph nodes and the SPLEEN) manufacture the blood cells the body needs, with extramedullary resources for ERYTHROCYTE production available as reserves from the LIVER, spleen (erythrocytes), and yellow BONE marrow. Researchers do not fully understand the mechanisms of hematopoiesis though know complex interactions of hormones, proteins, and chemicals regulate the processes by which the body makes new blood cells. There are two major divisions of hematopoiesis: erythropoiesis (production of erythrocytes) and leukopoiesis (production of leukocytes).

Pluripotency, Differentiation, and Proliferation

As best researchers understand the mechanisms of hematopoiesis, all blood cells arise from pluripotent BLOOD STEM CELLS that have the ability to develop into any of the blood cell types. The first level of hematopoiesis occurs when a blood stem cell either proliferates, extending the volume of pluripotent cells, or differentiates into one of two committed lineages, myeloid or lymphoid. The lymphoid lineage will produce lymphocytes and monocytes, and the myeloid lineage will produce erythrocytes, granulocytes (basophils, eosinophils, and neutrophils), and platelets. Each lineage generates a number of differentiations or stages of development. The length of time it takes for a pluripotent cell to produce a mature blood cell varies with the type of blood cell and other physiologic factors, ranging from 6 days for an erythrocyte to 14 days for a neutrophil.

Erythropoiesis

Erythropoiesis begins with committed myeloid cells that differentiate into myeloblasts or proerythrocytes. Myeloblasts will become granulocytes,

HEMATOPOIETIC STRUCTURES

Hematopoietic Structure	Blood Cells the Structure Produces
red BONE MARROW	erythrocytes, platelets, granulocytes, some monocytes
LIVER	erythrocytes on demand (extramedullary resource)
LYMPH nodes	lymphocytes, monocytes
SPLEEN	lymphocytes, monocytes erythrocytes on demand (extramedullary resource)
THYMUS	lymphocytes
yellow bone marrow	limited leukocytes erythrocytes and platelets on demand (extramedullary resource)

the majority of which will be neutrophils. Proerythrocytes will become erythrocytes (more than 99 percent) or platelets (less than 1 percent). Numerous substances influence and regulate erythropoiesis. Among them are

- ERYTHROPOIETIN (EPO), a HORMONE the KIDNEYS secrete that stimulates the bone marrow to increase differentiation of proerythrocytes and thus increase erythrocyte production
- intrinsic factor, or erythrocyte-maturing factor, which the STOMACH secretes to facilitate erythrocyte maturation
- vitamin B_{12}, also called extrinsic factor, which interacts with intrinsic factor
- iron, which is an essential component of HEMOGLOBIN (the protein complex within erythrocytes that binds with oxygen)

An erythrocyte goes through several stages of development before reaching a mature enough stage, that of reticulocyte, to leave the bone marrow. After 24 hours in circulation in the blood, the reticulocyte evolves to its final stage of maturity and becomes a fully functional erythrocyte. Erythrocytes circulate in the blood for about 120 days. The red bone marrow releases 2 million reticulocytes per minute into the blood circulation; the spleen extracts a comparable number of old erythrocytes from the circulation to maintain the correct proportion of erythrocytes in the blood.

Platelets arise from proerythrocytes that differentiate to become megakaryoblasts and then megakaryocytes. The megakaryocytes release fragments of their cytoplasm, which become platelets. While megakaryocytes are the largest cells in the bone marrow, platelets are the smallest particles in the blood. The spleen retains about 30 percent of the platelets the bone marrow produces, releasing them when a COAGULATION cascade sends chemical signals summoning platelets to the site of clot formation.

Leukopoiesis

Leukopoiesis, the production of white blood cells, takes place in both the bone marrow (granulocytes) and the lymph tissues (monocytes and lymphocytes). In general, all three types of leukocytes make up less than 1 percent of the blood cells in circulation. Many factors influence leukopoiesis, including immune status and whether an INFECTION is present in the body. Leukocytes also undergo a series of developmental evolutions before reaching maturity. Lymphocytes the lymph tissues release are immature and migrate to the THYMUS (T-cell lymphocytes) or the bone marrow (B-cell lymphocytes) to mature.

DISORDERS OF HEMATOPOIESIS

AMYLOIDOSIS	ANEMIA
BONE MARROW failure	LEUKEMIA
LEUKOPENIA	LYMPHOCYTOPENIA
LYMPHOMA	MULTIPLE MYELOMA
MYELODYSPLASIA SYNDROME	MYELOFIBROSIS
NEUTROPENIA	POLYCYTHEMIA VERA
THROMBOCYTHEMIA	THROMBOCYTOPENIA
vitamin B_{12} deficiency	

See also CELL STRUCTURE AND FUNCTION; HEMOLYSIS.

hemapheresis The process of withdrawing BLOOD from the body, filtering it through a machine called a cell separator to extract a desired blood component, and returning the rest of the blood to the person. There are two forms of hemapheresis, therapeutic and donor. Therapeutic hemapheresis, also called apheresis, removes damaged or defective components from the blood, which allows the body to naturally replace the components with healthy structures. Donor hemapheresis collects blood components for use in BLOOD TRANSFUSIONS.

CLINICAL APPLICATIONS FOR THERAPEUTIC HEMAPHERESIS

GLOMERULONEPHRITIS	GOODPASTURE'S SYNDROME
hyperviscosity	LEUKEMIA
MALARIA	MULTIPLE SCLEROSIS
MYASTHENIA GRAVIS	organ transplant rejection
PEMPHIGUS vulgaris	protein-bound DRUG toxicity
RHEUMATOID ARTHRITIS	SICKLE CELL DISEASE
thrombocytosis	thrombotic thrombocytopenic
transfusion reaction	PURPURA

For hemapheresis, the phlebotomist inserts an intravenous needle into a VEIN in each arm. One needle attaches to tubing that allows blood to flow out of the body and into the cell separator. The other needle attaches to tubing that brings the

blood back to the body after the cell separator has extracted the appropriate blood product. The entire process takes about two hours for most blood products. Some people find insertion of the needles uncomfortable and may also have chills and mild discomforts during the hemapheresis or for a short time afterward. There are relatively few risks with hemapheresis.

KINDS OF HEMAPHERESIS

cytapheresis	=	removal of cells
leukapheresis	=	removal of leukocytes (white blood cells)
plasmapheresis	=	removal of plasma
plateletapheresis	=	removal of platelets

See also BLOOD DONATION; HEMOCHROMATOSIS; PHLEBOTOMY.

hematoma Bleeding into the tissues that forms a contained mass. Most superficial hematomas are benign, such as the common hematoma auris, involving the auricle (outer EAR) and BLACK EYE, involving the orbital tissues surrounding the EYE. Such hematomas typically occur as the consequence of blows to the tissues that cause BLOOD vessels to break. As the blood coagulates the mass hardens. A hematoma may take weeks to several months to fully resolve as the body works to dismantle the clot. Most superficial hematomas do not require medical care, though a doctor should evaluate any injury that potentially involves the eye or symptoms of HEARING LOSS.

An internal hematoma that occurs within the skull (subdural or subarachnoid hematoma) is particularly dangerous and even life-threatening because it causes increased pressure that damages the BRAIN. Hematomas that occur within major organs such as the LIVER or the SPLEEN are also serious. These hematomas may be the result of trauma or may occur because of anomalous blood vessel structures (such as hemangioma) that spontaneously rupture. Internal hematomas require medical evaluation and careful monitoring. The doctor may recommend surgical removal of hematomas that threaten the function of vital organs such as the brain or the liver.

See also BRAIN HEMORRHAGE; ECCHYMOSIS; PETECHIAE; PURPURA; STROKE; TRAUMATIC BRAIN INJURY (TBI).

hemoglobin A combined protein within erythrocytes (red BLOOD cells) that is crucial to the OXYGEN–CARBON DIOXIDE EXCHANGE. Two proteins come together to form hemoglobin: heme, a reddish pigment that contains iron, and globin. Hemoglobin bonds loosely with oxygen and carbon dioxide molecules, depending on which is in higher concentration.

In the LUNGS, oxygen molecules have the higher concentration and bind with the hemoglobin. As the blood carries the erythrocytes deeper into the body where oxygen concentrations are lower, the bond becomes less stable. When the erythrocytes reach the CAPILLARY BEDS where the concentration of carbon dioxide is higher than the concentration of oxygen, the hemoglobin releases its oxygen molecules and replaces them with carbon dioxide molecules and carries the carbon dioxide back to the lungs where the exchange repeats.

Cigarette smoke contains high levels of carbon monoxide. Heavy smokers may have blood concentrations of carbon monoxide of 7 to 9 percent.

Carbon monoxide binds more strongly with hemoglobin than oxygen or carbon dioxide, forming a tight bond (the compound carboxyhemoglobin) that blocks hemoglobin from binding with either. Only small amounts of carbon monoxide inhaled into the lungs can interfere with the oxygen–carbon dioxide exchange significantly enough to cause poisoning (HYPOXIA) or death. Carbon monoxide begins to cause symptoms of oxygen deprivation when its blood concentration reaches 10 percent, impairs neurologic function at 30 percent, and can cause death at 50 percent. A gas commonly present in the environment, carbon monoxide is a byproduct of incomplete combustion.

See also ANEMIA; HEMOCHROMATOSIS; INHALED TOXINS; SICKLE CELL DISEASE; SMOKING AND HEALTH; THALASSEMIA.

hemolysis The destruction and disassembly of erythrocytes (red BLOOD cells). Erythrocytes live in the blood for about 120 days after their release from the BONE MARROW. At the end of this time they either die or the SPLEEN culls them from circu-

lation. The spleen partially dismantles the erythrocytes, reducing toxic heme into BILIRUBIN that the body excretes with the BILE. The LIVER then recycles these components for numerous other uses in the body. Accelerated hemolysis, which results in ANEMIA, can occur with, or characterizes, various disorders.

CONDITIONS IN WHICH HEMOLYSIS MAY OCCUR

adverse DRUG reactions	BLOOD enzyme disorders
BLOOD TRANSFUSION reaction	ERYTHROCYTE metabolic disorders
HEMOGLOBIN disorders	IMMUNE SYSTEM dysfunction
SEPTICEMIA	SICKLE CELL DISEASE
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	THALASSEMIA

See also APOPTOSIS; CELL STRUCTURE AND FUNCTION; PHAGOCYTOSIS; SPLENOMEGALY.

hemophilia A group of inherited GENETIC DISORDERS in which certain CLOTTING FACTORS are deficient or absent, resulting in clotting dysfunction. People who have hemophilia tend to bleed easily and longer than normal. Some forms of hemophilia carry substantial risk for life-threatening hemorrhage (bleeding).

Types of hemophilia Doctors classify hemophilia according to the deficient clotting factor, which may be missing from the BLOOD, present in subnormal quantities, or present but defective. About 85 percent of people who have hemophilia have hemophilia A, a deficiency of clotting factor VIII (also called antihemophilic factor A). The remaining 15 percent have hemophilia B, a deficiency of clotting factor IX (also called Christmas factor, antihemophilic factor B, or PLASMA thromboplastin). Hemophilia B was once called Christmas disease—named after the family in which doctors first identified the clotting factor IX deficiency—and distinguished this type of hemophilia from the classic hemophilia A. Hemophilia C, which is very rare in the United States, is a deficiency of clotting factor XI (also called plasma thromboplastin antecedent).

Inheritance patterns The most common types of hemophilia, hemophilia A and hemophilia B, are inherited X-linked CHROMOSOMAL DISORDERS, meaning they nearly always only affect males. The daughters of a man who has hemophilia A or B will all carry the defective GENE, though the sons will have normal clotting factor genes. The son of a carrier has a 50 percent chance of having hemophilia; the daughter of a carrier has a 50 percent chance of also carrying the defective genes. Rarely, hemophilia A or B occurs through spontaneous gene MUTATION. In such circumstances it is possible for a woman to have the disorder. Hemophilia C, which primarily affects people who are of Ashkenazi Jewish descent, is an autosomal disorder that affects men and women equally though is very rare.

Symptoms and Diagnostic Path

Excessive bleeding is the most common symptom of hemophilia A or B, which often first manifests after CIRCUMCISION. The more severe the hemophilia, the earlier in life symptoms become apparent. Some men may not experience symptoms until adulthood, while others experience life-threatening hemorrhage with common childhood injuries such as nosebleed (EPISTAXIS) and trauma such as a cut. The diagnostic path includes blood tests that measure clotting times, PLATELET AGGREGATION, blood cell counts, and the presence of clotting factors VIII, IX, and XI, and the von Willebrand factor. The findings of these tests, along with personal and family medical histories, are generally conclusive of the diagnosis.

The amount of functional clotting factor in the blood determines the severity of the hemophilia. Clotting factor presence above 10 percent generally produces only mild to moderate symptoms; clotting factor presence below 1 percent, which occurs in about 70 percent of people who have hemophilia, generally produces severe symptoms. Life-threatening hemorrhage is the most significant consequence of hemophilia.

Treatment Options and Outlook

The goal of treatment is generally to raise the deficient clotting factor to 30 percent, or 50 to 100 percent during episodes of active bleeding, depending on the site. Treatment may be transfusions with fresh frozen plasma or plasma cryoprecipitate, both of which contain clotting factors VIII and IX, or with clotting factor concentrates. The more often these treatments are necessary, however, the greater the likelihood the person will

develop antibodies to the clotting factors that subsequently prevents these treatments from having any effect. In such situations the doctor may administer porcine-derived forms of clotting factor VIII or prothrombin complex concentrate, which bypass some of the steps in the coagulation cascade to avoid ANTIBODY activation.

A promising treatment for mild hemophilia A is the synthetic HORMONE desmopressin. Also called DDAVP, desmopressin is an analog (close chemical relative) of the endogenous hormone vasopressin, which the PITUITARY GLAND secretes. Administered intravenously or via nasal spray, desmopressin causes the body to increase blood levels of clotting factors VIII and IX. However, desmopressin has little effect in people who have hemophilia B. Desmopressin may affect other aspects of the coagulation cascade and can elevate the BLOOD PRESSURE.

Blood product treatments for hemophilia carry the risk of INFECTION with various pathogens that current blood screening technology cannot detect including HEPATITIS A, human T-lymphotropic virus 1 (HTLV-1), west Nile virus, MALARIA, and also CYTOMEGALOVIRUS (CMV). Though infection with human immunodeficiency virus (HIV) was a significant problem during the 1980s, screening procedures in effect today have nearly eliminated the risk for acquiring HIV/AIDS through donated blood products.

Many people who have hemophilia are able to enjoy a high QUALITY OF LIFE with ongoing medical monitoring and lifestyle choices to reduce the risk for traumatic injury. However, complications such as JOINT damage due to frequent bleeding can limit physical activities. GASTROINTESTINAL BLEEDING is also a potential complication.

Risk Factors and Preventive Measures

Genetic inheritance is the only known risk factor for hemophilia. Health experts encourage people who have hemophilia, know they carry the gene defect for hemophilia, or have a family history of unusual bleeding to discuss FAMILY PLANNING with a genetic counselor who can advise of the risks that children will either carry or have hemophilia. Much research currently focuses on perfecting recombinant technologies to provide clotting factor therapies free from risk of infection and antibody development. Other research efforts are exploring the potential for GENE THERAPY that can repair the damaged genes, though this potential has not yet yielded practical results.

See also ANTIBODY; COAGULATION; GENETIC COUNSELING; GENETIC DISORDERS; INHERITANCE PATTERNS; VON WILLEBRAND'S DISEASE.

leukapheresis See HEMAPHERESIS.

leukemia A type of CANCER that affects the BONE marrow's production of leukocytes (white BLOOD cells). Doctors classify leukemia as either myeloid (sometimes called myelocytic) or lymphocytic (sometimes called lymphoblastic), depending on the type of leukocytes affected. Within either classification leukemia can be acute or chronic. The four most common types of leukemia are

- acute lymphocytic leukemia (ALL)
- chronic lymphocytic leukemia (CLL)
- acute myeloid leukemia (AML)
- chronic myeloid leukemia (CML)

LEUKEMIA VS. LYMPHOMA

LYMPHOMA is another type of cancer that can affect the lymphocytes. However, lymphoma is a cancer of the lymphatic tissues that produce and store lymphocytes. Leukemia is a cancer of the BONE MARROW that alters the development and proliferation of the lymphocytes that enter the BLOOD circulation.

There are a number of subtypes within these classifications, usually identified according to the affected cell type or its developmental stage. Though common perception is that leukemia primarily affects children, 10 times as many adults as children develop this type of cancer. Children are more likely to develop acute leukemia and adults over age 60 to develop chronic leukemia, though either form can occur at any age. Some forms of childhood leukemia are fully curable and some forms of adult leukemia are highly manageable. GENETIC PREDISPOSITION and certain environmental factors, such as exposure to industrial chemicals, pesticides, and RADIATION THERAPY or CHEMOTHERAPY, appear to increase an individual's risk for developing leukemia. However, most of the time doctors do not know what causes this leukemia to develop.

How Leukemia Develops

All blood cells arise from pluripotent BLOOD STEM CELLS, "parent" cells within the BONE MARROW that have the ability to form into several different kinds of blood cells. A complex interaction of genetic encoding, chemicals, proteins, molecular functions, and physiologic needs determines the manner in which blood stem cells differentiate (become specific kinds of cells) and proliferate (reproduce themselves). At the first level of differentiation, a blood stem cell establishes its lineage as lymphoid or myeloid. Myeloid stem cells give rise to erythrocytes, platelets, granulocytes, and monocytes. Lymphoid stem cells give rise to lymphocytes. In leukemia, the stem cells are normal though something goes awry at the first stage of differentiation, and one of the lines—lymphoid or myeloid—produces abnormal cells.

In acute forms of leukemia the bone marrow accelerates LEUKOCYTE production and releases immature leukocytes not yet capable of functioning as leukocytes. In relatively short time the immature cells flood the bone marrow, crowding out other cells. The onset of symptoms with acute leukemia is generally rapid because the immature cells the bone marrow releases cannot function yet are entering the circulation at a rate that causes them to quickly become dominant in the blood. In chronic leukemia the bone marrow's rate of production is normal and the leukocytes the marrow releases into the circulation are mature but defective. The onset of symptoms in

chronic leukemia is usually gradual because these cells, though defective, can function to some extent and enter the blood circulation at the normal rate. In all types of leukemia, the defective cells also block the bone marrow from producing platelets and erythrocytes, resulting in dysfunctional COAGULATION (clotting) and ANEMIA.

Acute lymphatic leukemia (ALL) The most common leukemia of childhood, ALL arises when a genetically damaged lymphoid clone cell in the bone marrow proliferates, causing immature lymphocytes, called lymphoblasts or leukemic blasts, to replace healthy lymphocytes in the bone marrow and the blood circulation. The accumulation prevents normal HEMATOPOIESIS, resulting in anemia, coagulation dysfunction, and vulnerability to INFECTION. About 85 percent of ALL involves B-cell lymphocytes and the remaining 15 percent involves T-cell lymphocytes. Doctors diagnose about 4,000 people a year with ALL in the United States.

Chronic lymphatic leukemia (CLL) Doctors diagnose about 8,000 people a year with CLL in the United States, more than 75 percent of them being over the age of 60. In CLL, the proliferating defective lymphocytes function normally. CLL may generate no symptoms or ill effects, in which case doctors generally opt for watchful waiting as the treatment approach. As CLL progresses, however, it causes dysfunctional IMMUNE RESPONSE. Defective lymphocytes that accumulate in the bone marrow eventually suppress bone marrow function.

Acute myeloid leukemia (AML) The most common leukemia among people over age 40, AML arises through the proliferation of a defective myeloid clone cell and manifests in one of seven forms. Doctors designate these forms as subtypes M1 through M7, according to the cells involved. The subtype determines the course of treatment and likelihood for REMISSION. As with ALL, the proliferation of the defective clone prevents normal hematopoiesis with consequent THROMBOCYTOPENIA, anemia, and often NEUTROPENIA. Doctors diagnose about 12,000 people a year with AML in the United States.

Chronic myeloid leukemia (CML) Nearly always a cancer occurring in adulthood, CML results from the translocation of chromosomes 9 and 22, an acquired MUTATION commonly referred to as the Philadelphia, or Ph, CHROMOSOME. Researchers do not know what causes the abnormality, which produces the rampant proliferation of monocytes or granulocytes that function normally. Other hematopoiesis is normal as well. Doctors diagnose about 54,000 people a year with CML in the United States.

Symptoms and Diagnostic Path

Symptoms of leukemia develop when the cancerous cells in the blood circulation begin to outnumber the healthy cells. Early symptoms are insidious and often mimic those of common viral infections. As the leukemia progresses, symptoms become more pronounced and typically include

- unexplained low-grade FEVER
- general malaise or lethargy
- PAIN in the joints
- unintended weight loss
- sweating at night
- loss of APPETITE
- tiredness or fatigue
- easy bleeding or bruising, or the appearance of PETECHIAE (pinpoint hemorrhages beneath the SKIN)

The diagnostic path typically includes physical examination, diagnostic blood tests, and bone marrow biopsy. The physical examination may reveal SPLENOMEGALY (swollen SPLEEN) and LYMPHADENOPATHY (swollen lymph nodes). Characteristic patterns of abnormal cell counts and structures identify the different types of leukemia. In addition to abnormalities in the leukocytes, depletion of erythrocytes and platelets is common. Bone marrow biopsy confirms the diagnosis. Specialized laboratory tests, such as cytologic examination and immunophenotyping, establish the characteristics of the abnormal cells to identify the type of leukemia.

Treatment Options and Outlook

Treatment regimens for leukemia vary with the type of leukemia, the person's age, and the person's general health status aside from the leukemia. Chemotherapy and RADIATION THERAPY,

separately or in combination, remain the mainstay of the therapeutic arsenal, with the objective being to establish remission (a state in which there is no evidence of the leukemia and all blood counts and blood cells are normal). Oncologists use several staging systems for leukemia to identify the kinds of cells, cell lineage, and cell counts.

Chemotherapy is the treatment of choice, with blood stem cell or BONE MARROW TRANSPLANTATION sometimes an option depending on the leukemia's characteristics and stage at the time of diagnosis. Research continues to produce new chemotherapy agents and new combinations of existing agents that appear more successful, though their ability to sustain remission over time remains unknown. The initial phase of chemotherapy typically involves cycles of chemotherapy drugs administered over a period of one to two years, with maintenance oral chemotherapy drugs for another two and a half to three years for ALL. Oncologists may use radiation therapy to treat accumulations of cancerous lymphocytes in the BRAIN, spleen, and lymph nodes such as may occur with ALL. Many people need supplemental BLOOD TRANSFUSION and ANTIBIOTIC MEDICATIONS during chemotherapy.

CHEMOTHERAPY DRUGS USED TO TREAT LEUKEMIA

2-chlorodeoxyadenosine	5-azacytidine
6-thioguanine	anthracycline
arsenic trioxide	calicheamicin
carboplatin	hlorambucil
cladribine	conjugated MONOCLONAL ANTIBODIES (MABS)
cyclophosphamide	cytarabine
daunorubicin	dexamethasone
daunorubicin	fludarabine
hydroxyurea	idarubicin
ifosfamide	imatinib
interferon	L-asparaginase
melphalan	mercaptopurine
methotrexate	mitoxantrone
pentostatin	prednisolone
prednisone	teniposide
topotecan	vindesine
vincristine	

Across all types of leukemia, about 65 percent of people achieve initial remission with treatment. The rate of sustained remission (five years or longer) is much higher with acute than with chronic forms of leukemia, and in younger (under age 14 years) than older (over age 60) people. For children under age 14 who undergo treatment for ALL, about 80 percent achieve long-term remission such that doctors consider them cured of the leukemia. About 30 percent of adults who have ALL achieve similar long-term remission. Because successful treatment regimens are relatively new, however, doctors do not know what potential health complications, if any, may arise decades after treatment. Long-term survival rates are higher for lymphocytic leukemias than for myeloid leukemias.

Risk Factors and Preventive Measures

The causes of leukemia remain mostly unknown. Doctors do know that about 60 percent of people who have myelodysplasia syndrome eventually develop AML. As well, people who have first-degree relatives (parent, sibling, or child) who acquire ALL are about four times more likely to develop ALL themselves. Researchers have identified a number of potential risk factors associated with leukemia, though the extent and nature of the associations remains unclear. Among them are

- exposure to high-DOSE radiation, including radiation therapy
- previous chemotherapy for other kinds of cancer
- exposure to the industrial chemicals benzene and formaldehyde and their derivative compounds
- cigarette smoking
- infection with human T-cell leukemia virus 1 (HTLV-1)
- DOWN SYNDROME and CHROMOSOMAL DISORDERS that run in families

Most people who develop leukemia do not have any history of exposure to suspected risk factors, however, making prevention recommendations difficult. There are no known methods for preventing leukemia.

See also B-CELL LYMPHOCYTE; CANCER TREATMENT OPTIONS AND DECISIONS; ENVIRONMENTAL HAZARD EXPOSURE; ERYTHROPOIETIN (EPO); LYMPHOMA; MULTIPLE

MYELOMA; SIGNS AND SYMPTOMS OF CANCER; SMOKING AND HEALTH; STAGING AND GRADING OF CANCER.

leukocyte A white BLOOD cell, also referred to as a WBC. Leukocytes are the foundation of the body's IMMUNE RESPONSE and are phagocytic—that is, they have the ability to consume other cells. They circulate in the blood and the LYMPH as well as reside in tissues throughout the body. There are three basic types of leukocytes: granulocytes, monocytes, and lymphocytes. Each type has several subtypes. The SPLEEN and lymph tissues produce monocytes and lymphocytes; the red BONE MARROW produces granulocytes.

HEALTH CONDITIONS THAT AFFECT LEUKOCYTE COUNTS

ALLERGY response	ASTHMA
AUTOIMMUNE DISORDERS	CHEMOTHERAPY
environmental toxin exposure	HYPERSENSITIVITY REACTION
INFECTION	INFLAMMATION
LEUKEMIA	LEUKOPENIA
LYMPHOCYTOPENIA	LYMPHOMA
many cancers	medication side effects
MONONUCLEOSIS, INFECTIOUS	RADIATION THERAPY
surgery	vitamin B_{12} deficiency

A healthy adult has between 5,000 and 10,000 leukocytes per microliter of blood, with granulocytes accounting for about 70 percent. Increases in certain subtypes of leukocytes suggest particular health conditions. A substantial increase overall in LEUKOCYTE count may indicate a cancer of the bone marrow such as LEUKEMIA or LYMPHOMA. The ratio between erythrocytes (red blood cells) and leukocytes in the blood is also an important diagnostic indicator.

For further discussion of leukocytes within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also B-CELL LYMPHOCYTE; CELL STRUCTURE AND FUNCTION; ERYTHROCYTE; HEMATOPOIESIS; PHAGOCYTOSIS; PLASMA; PLATELET; SIDE EFFECT; THYMUS.

leukopenia A decline in the number of leukocytes (white BLOOD cells) circulating in the blood to fewer than 4,000 leukocytes per microliter of whole blood. The most common manifestation of leukopenia is NEUTROPENIA, a shortage of granulocytes called neutrophils. Most leukopenia is secondary to other health conditions a person may have, such as viral infections or cancers that involve the BONE MARROW, and circumstances, such as CHEMOTHERAPY. Numerous medications can cause leukopenia as an undesired SIDE EFFECT of treatment. In such situations the doctor will evaluate the relative value of the inherent risks in continuing or discontinuing the causative medication. Leukopenia lowers the body's ability to resist and fight INFECTION and when severe can allow life-threatening infections to invade. Frequent or unusual infections, especially persistent GINGIVITIS or periodontitis, may suggest leukopenia. Treatment targets any infection or other underlying cause.

See also LYMPHOCYTOPENIA; PERIODONTAL DISEASE; THROMBOCYTOPENIA.

LEUKOCYTES

Type of Leukocyte	Subtypes	Organ that Produces
granulocytes	basophils, eosinophils, neutrophils	red BONE MARROW
monocytes	macrophages (reside in the tissues)	SPLEEN, lymph nodes
lymphocytes	T-cell lymphocytes	SPLEEN, lymph nodes, THYMUS
	cytotoxic T-cells	
	helper T-cells	
	memory T-cells	
	suppressor T-cells	
	B-cell lymphocytes	
	memory B-cells	
	PLASMA cells	

lymph The fluid that circulates through the LYMPH VESSELS. Lymph is clear and colorless or white with fat, depending on its location. It contains about 90 percent water and carries proteins, globulins, GLUCOSE, electrolytes, and other chemicals dissolved within it. Leukocytes, primarily lymphocytes and monocytes, circulate in the lymph, suspended in the fluid. Lymph originates from and returns to the BLOOD. Fluid from the blood (PLASMA) seeps from the capillaries into the spaces between the cells. This interstitial fluid carries the NUTRIENTS from the blood, surrounding the cells in a bath from which they withdraw the nutrients they need. Leukocytes in the blood move freely between the lymph and the blood. Lymph capillaries draw the interstitial fluid back into the lymph vessels, which carry the lymph they collect through a network of lymph vessels. Ultimately the lymph vessels return the lymph to the blood via its portals into the right and left subclavian veins.

Compared to the blood the HEART pumps through the circulation, the lymph moves leisurely through its network of vessels, achieving a top rate of about 100 milliliters an hour in the major trunk vessels (the lymphatic ducts). It flows primarily as a function of gravity, with some help from the massaging actions of contracting skeletal muscles during movement. Because most of the body's INFECTION-fighting action takes place in the lymph nodes and other lymph tissues, the lymph is the primary pathway for transporting pathogens for destruction by macrophages and other leukocytes in the lymph nodes. The lymph also is the primary channel for the body to carry the residue of infection to other structures and systems that eliminate it from the body (through phagocytosis as well as other means). CANCER cells can overload the lymph, hijacking it to become the pathway for their spread (METASTASIS) to other organs and parts of the body.

For further discussion of the lymph within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also CISTERNA CHYLI; LYMPH NODE; RIGHT LYMPHATIC DUCT; THORACIC DUCT.

lymphadenitis INFLAMMATION or INFECTION of LYMPH nodes. Lymphadenitis characterizes systemic infections such as infectious mononucleosis and regional infections such as SEXUALLY TRANSMITTED DISEASES (STDS). It may affect any lymph nodes in the body though is most noticeable when it affects LYMPH NODE clusters near the surface of the SKIN, such as in the neck, axillae (underarms), and groin (inguinal). The typical symptoms of lymphadenitis are palpable lymph nodes that may range in size from that of a small pea to that of a large marble. The swellings are often painful, and the skin above the area may be reddened (erythematous) and warm to the touch when infection of the lymph nodes themselves is the cause. Diagnosis may require lymph node biopsy when there are no clear signs of infection or when lymphadenitis continues beyond six weeks.

Lymphadenitis without signs of infection may indicate cancer, either affecting the lymph structures (LYMPHOMA) or in METASTASIS from any location in the body. Pathogens or cancer cells traveling through the lymph can initiate such a massive activation of phagocytic response that the resulting action of macrophages and lymphocytes overwhelms the lymph nodes with cellular debris faster than the lymph can carry it away.

See also LYMPH VESSELS; MONONUCLEAR PHAGOCYTE SYSTEM; MONONUCLEOSIS, INFECTIOUS; PHAGOCYTOSIS.

lymphadenopathy Swelling and enlargement of the LYMPH nodes. Lymphadenopathy indicates that the affected lymph nodes are fighting an INFECTION in nearby tissues, and the enlargement is most often benign and normal. A common manifestation of lymphadenopathy is swollen lymph nodes in the neck when a person has a sore THROAT, or under the arm when there is a cut or bruise on the hand or arm. The swollen lymph nodes typically feel firm to the touch and may hurt. As the underlying infection improves, the swelling retreats, and the lymph nodes return to normal size. When lymph nodes throughout the body are swollen, the underlying cause is likely a systemic infection such as a VIRUS. Occasionally persistent lymphadenopathy suggests LYMPHOMA or LEUKEMIA, cancers of the lymph tissues or BONE MARROW.

See also LYMPHADENITIS; LYMPH NODE.

lymphangioma A noncancerous LESION made up of LYMPH VESSELS. Pathologically, doctors classify a

lymphangioma as hamartomatous, (harmartomas are benign tumors) which refers to the lesion's pattern of self-limiting growth. Lymphangiomas are congenital or arise soon after birth, most commonly manifesting as SKIN lesions on the head, back, arms, and legs, though the lesions may involve any external or internal epithelial tissue (skin and mucous membranes). Lymphangiomas grow slowly, then stop growing and remain the same size. Though not cancerous, a lymphangioma may cause problems or symptoms because of its location and size. A lymphangioma in the SMALL INTESTINE, for example, may interfere with the absorption of NUTRIENTS or create an ILEUS (obstruction).

Lymphangiomas that do not cause symptoms do not require treatment as they are self-limiting. A surgeon can operate to remove a lymphangioma that causes symptoms or is cosmetically unsatisfactory. However, the structure of a lymphangioma has no capsule and tends to diffusely infiltrate tissue, making it difficult for the surgeon to remove it completely. If the lymphangioma has not finished growing, it will recur. Most lymphangiomas are benign in that they do not cause symptoms or health problems.

See also BIRTHMARK; HEMANGIOMA.

lymphedema Swelling and often discomfort arising from inadequate LYMPH drainage and flow that allows interstitial fluid (fluid between the cells) to accumulate. Lymphedema most often occurs when INFECTION or CANCER that extensively engages the lymphatic system, or when surgery disrupts the LYMPH VESSELS and lymph nodes. Lymphedema is a common consequence of surgery and RADIATION THERAPY as treatments for cancer. Surgeons typically remove adjacent or sentinel lymph nodes, which are most likely to be affected by the cancer, during surgery to remove cancerous tumors to determine the extent to which the cancer has penetrated the tissues or metastasized (spread) to other tissues. Lymphedema can be debilitating when the swelling becomes substantial. Recurrent, progressive lymphedema often develops into fibrosclerosis (scarring and hardening) of the involved tissues.

It is important to distinguish lymphedema from other causes of swelling, such as edema (simple fluid retention) and ASCITES, because though the appearance of the affected area may be similar the treatment approaches differ. In chronic lymphedema the SKIN over the swollen area acquires a characteristic "orange peel" texture, which indicates damage to the underlying tissue. Tissue in the damaged area becomes susceptible to infection and ulceration, as the lymphedema compromises its BLOOD circulation and immune response. While conventional edema improves with diuretic medications, lymphedema does not.

For lymphedema, treatment focuses on improving the flow of fluid into and through the lymph vessels. Compression sleeves and stockings provide gentle, consistent pressure against the affected arm or leg, helping prevent interstitial fluid from accumulating. Some people with severe lymphedema benefit from compression pump therapy, in which a pump gently inflates and deflates pressure cuffs wrapped around the arms or legs, to help squeeze interstitial fluid into the lymph capillaries. Surgery to remove damaged portions of tissue and lymphatic structures is a treatment of end resort that may improve very severe lymphedema when other methods have failed, though itself can cause further or more extensive damage.

Lymphedema is a lifelong concern for most people who develop it, regardless of its cause though particularly after extensive surgery that disrupts the lymphatic structures or in which the surgeon removes lymph nodes. Many people can manage their symptoms and discomfort through preventive measures such as frequent movement or self-massage of involved areas and prompt therapeutic response when swelling begins.

See also HEART FAILURE; LYMPH NODE; SENTINEL LYMPH NODE DISSECTION; SURGERY BENEFIT AND RISK ASSESSMENT.

lymph node A small structure of lymphatic tissue. LYMPH nodes, sometimes erroneously called lymph glands, occur individually as well as in beadlike strings within the tissues. The lymph nodes range in size from that of a grain of rice to that of a kidney bean, and appear roughly kidney shaped.

Each lymph node contains high numbers of lymphocytes and macrophages (tissue-resident monocytes), which filter pathogens and cellular

debris from the lymph. Follicles within the lymph node contain B-cells and T-cells, which proliferate and mature in the follicles. The B-cells produce antibodies specific to the antigens the lymph carries into the lymph node. The lymph node adds these antibodies to the lymph as the lymph exits the node. The lymph node's follicles release additional T-cells as necessary to fight INFECTION, responding to chemicals PHAGOCYTOSIS releases. Extensive networks of lymphatic capillaries carry lymph among the lymph nodes as well as to and from the larger LYMPH VESSELS.

Lymph nodes commonly swell when they are actively responding to infection because they fill with the pathogenic cells they filter from the lymph, a circumstance doctors call LYMPHADENOPATHY. LYMPHADENITIS occurs when the infection involves the lymph node itself. The lymph nodes also can become seeding sites for cancer cells that are metastasizing (spreading) to other parts of the body. Most operations to remove cancerous tumors also include removal of adjacent lymph nodes to examine them for the presence of cancer cells, which is key to the STAGING AND GRADING OF CANCER.

See also ANTIBODY; ANTIGEN; LYMPHEDEMA; METASTASIS; PATHOGEN; SENTINEL LYMPH NODE DISSECTION.

lymphocyte A type of LEUKOCYTE (white BLOOD cell) that primarily resides in the LYMPH and lymph tissues. Lymphocytes are the body's primary immune defense and move through the lymph in response to antigens and pathogens. When more rapid deployment is necessary, lymphocytes enter the bloodstream. About 1 percent of the body's lymphocyte population circulates in the blood, making up about 25 percent of the circulating leukocytes. There are two major types of lymphocytes—T-cells and B-cells—and natural killer cells. Each type has different immune responsibilities.

T-Cells

T-cells, which make up about 75 percent of lymphocytes, originate in the BONE MARROW and migrate to the THYMUS to come to maturity. In the thymus T-cells acquire the ability to distinguish between "self" and "nonself," an essential function of determining whether the particles the T-cells encounter are invaders. Mature T-cells carry kinds of antibodies, identified as CLUSTERS OF DIFFERENTIATION, that denote the T-cell's immune function. There are numerous subtypes of T-cells, the most common being

- helper T-cells, which secrete a cytokine called CD4 (for cluster of differentiation 4) that directs the response of other T-cells
- cytotoxic T-cells, which attack invading cells by releasing chemicals that penetrate their cell membranes, which causes them to rupture and die
- suppressor T-cells, which reign in the IMMUNE RESPONSE after the immune attack has squelched the threat
- memory T-cells, which retain the ability to produce antibodies against the same ANTIGEN should it reappear in the body

B-Cells

B-cells, which make up about 10 percent of lymphocytes, originate in the bone marrow and migrate to the lymph tissues to come to maturity and await activation via contact with an antigen. When such contact occurs, the individual B-cell develops antibodies specific to the antigen, differentiates into either a memory B-cell or a PLASMA cell and then proliferates within the lymph tissues, lymph, and bloodstream. Memory cells "remember" the specific antigen and produce antibodies whenever the antigen again enters the body. This process provides long-term protection against pathogens. Plasma cells generate copious antibodies as they replicate, providing an immediate immune response to the PATHOGEN.

Natural Killer Cells

Natural killer (NK) cells are specialized lymphocytes that attack and destroy self cells that have become defective in some way. Researchers believe one function of NK cells is to attack tumors as they are beginning to develop, preventing them from taking root. NK cells also appear to attack cells that viruses hijack, preventing the VIRUS from replicating and causing infection.

For further discussion of lymphocytes within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also B-CELL LYMPHOCYTE; CELL STRUCTURE AND FUNCTION; GRANULOCYTE; HEMATOPOIESIS; LYMPHOMA; MONOCYTE; MULTIPLE MYELOMA; NATURAL KILLER (NK) CELL; THYMECTOMY.

lymphocytopenia A decline in the number of lymphocytes in the BLOOD to fewer than 1,000 lymphocytes per microliter of whole blood. Lymphocytes circulate in the blood and the LYMPH, their primary role being to identify and attack invading pathogens to prevent and fight INFECTION. Lymphocytopenia often accompanies IMMUNODEFICIENCY disorders, notably HIV/AIDS (in which it may be one of the earliest indications of infection), infections such as TUBERCULOSIS and HEPATIS, and AUTOIMMUNE DISORDERS such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) and MYASTHENIA GRAVIS. Other causes include RADIATION THERAPY as cancer treatment, long-term PUVA (psoralen plus ultraviolet light of A wavelength) PHOTOTHERAPY for treatment of PSORIASIS, severe stress, and medications such as CORTICOSTEROID MEDICATIONS. Lymphocytopenia may be transitory, with the LYMPHOCYTE level returning to normal when the underlying cause improves. Depending on the cause, people who have lymphocytopenia may show few symptoms. Treatment targets the underlying condition. The health consequences of lymphocytopenia vary with the overall status of the IMMUNE SYSTEM.

See also LEUKOPENIA; NEUTROPENIA; THROMBOCYTOPENIA.

lymphoma A type of CANCER that affects the hematopoietic functions of the LYMPH system that results in the uncontrolled proliferation of lymphocytes, the type of LEUKOCYTE (white BLOOD cell) that the lymph tissues primarily produce. The lymphocytes congregate in the lymph tissues to form tumors.

LYMPHOMA VS. LEUKEMIA

LEUKEMIA and LYMPHOMA are both cancers that can affect the lymphocytes. However, leukemia is a CANCER of the BONE MARROW that alters the development and proliferation of lymphocytes that enter the BLOOD circulation. Lymphoma is a cancer of the lymphatic tissues that produce lymphocytes.

Though there are nearly three dozen identified types of lymphoma doctors assign them to one of two major categories, Hodgkin's lymphoma and non-Hodgkin's lymphoma. Doctors diagnose about 60,000 people with lymphoma in the United States each year. Lymphoma is the fifth most common kind of cancer among American adults and the third most common kind of cancer among children.

How Lymphoma Develops

Lymphomas originate in the reticuloendothelial or clone cells in the lymph structures that produce lymphocytes, notably the lymph nodes and the SPLEEN. Most lymphomas affect B-cell lymphocytes (B-cells) though some affect T-cell lymphocytes (T-cells). Hodgkin's lymphoma involves a specific kind of B-cell called a Reed-Sternberg cell. In all lymphomas, the affected lymphocytes proliferate and migrate to lymph tissues, such as lymph nodes and the spleen. The lymphocytes cluster into tumorous formations that drain the NUTRIENTS and other resources healthy cells require, causing the healthy cells to die and allowing the cancerous lymphocytes to continue proliferating.

A key marker for the extent and severity of lymphoma is whether tumors are present on only one side or on both sides of the DIAPHRAGM. Lymphomas present only on one side of the diaphragm (either above or below) tend to be less aggressive than those that are present in LYMPH NODE regions on both sides of the diaphragm, as well as more responsive to treatment (particularly those above the diaphragm). Cancerous lymphocytes can also metastasize to other kinds of tissues throughout the body, primarily traveling through the lymphatic system. The most common sites for lymphoma METASTASIS outside the lymphatic system are the BRAIN, SKIN, BONE, and BONE MARROW. However, because the lymphatic network extends throughout the interstitial tissues, metastases in advanced disease can appear anywhere.

Hodgkin's Lymphoma

Hodgkin's lymphoma, also called Hodgkin's disease, accounts for about 15 percent of diagnosed lymphomas. It most commonly affects people between ages 16 to 34 and over age 55. The presence of specifically abnormal B-cells, Reed-Sternberg cells, is the hallmark of Hodgkin's lymphoma.

There are five identified subtypes of Hodgkin's lymphoma:

- lymphocyte-predominant (also called nodular lymphocyte predominance)
- nodular sclerosis
- lymphocyte-rich (also called classical)
- mixed cellularity
- lymphocyte-depleted

Treatment regimens and prognoses differ for each subtype. Nodular sclerosis Hodgkin's lymphoma is the most common subtype, accounting for about two thirds of diagnoses, and tends to be moderately progressive. Lymphocyte-predominant Hodgkin's lymphoma tends to progress slowly; lymphocyte-depleted Hodgkin's lymphoma tends to be quite aggressive with rapid progression and frequent metastasis to organs outside the lymphatic system. In general, the higher the number of Reed-Sternberg cells, the more aggressive the cancer.

Non-Hodgkin's Lymphoma

The non-Hodgkin's lymphomas account for about 85 percent of diagnosed lymphoma and most commonly affect people over age 60, though can develop at any age. There are several dozen subtypes of non-Hodgkin's lymphoma, currently classified according to the type of tumor (also called a neoplasm) and its characteristics. Doctors further classify non-Hodgkin's lymphomas as to whether they are aggressive (rapidly growing)—high or intermediate grade—or indolent (slow growing)—low grade.

NON-HODGKIN'S LYMPHOMA SUBTYPES

AIDS-related	anaplastic large cell
angioimmunoblastic	blastic natural killer (NK)
BONE	Burkitt's
CENTRAL NERVOUS SYSTEM (CNS)	cutaneous T-cell
diffuse large cell	diffuse small noncleaved cell
eyelid	follicular
immunoblastic	lymphoblastic
lymphoplasmacytic	mantle cell
marginal zone	MUCOSA-ASSOCIATED LYMPHOID
mycosis fungoides	TISSUE (MALT)
nodal marginal zone	nasal NK/T
small lymphocytic	ocular (EYE)
splenic marginal zone	

Symptoms and Diagnostic Path

Many people do not have symptoms of lymphoma at the time of diagnosis. Rather, the doctor detects characteristic abnormalities in diagnostic blood tests conducted for other reasons, often as part of a ROUTINE MEDICAL EXAMINATION. When symptoms are present they can be vague and generalized, typical of common viral infections though they tend to persist or recur rather than resolving. Such symptoms may include

- painless swellings in the lymph nodes, most noticeable in the axillae (underarms), neck, or groin (LYMPHADENOPATHY)
- unexplained, frequent fevers
- unintended or unexplained weight loss
- profuse sweating at night
- tiredness, fatigue, or lethargy
- unexplained, generalized itching (PRURITUS)

The diagnostic path begins with the doctor's physical examination, which may reveal SPLENOMEGALY (enlarged spleen) or detect enlarged lymph nodes beneath the collarbone or in the abdomen. Diagnostic blood tests and bone marrow biopsy demonstrate the proliferation of lymphocytes. Other diagnostic procedures the oncologist may conduct include tissue biopsy of swellings, COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to detect the presence of tumors deep within the body, POSITRON EMISSION TOMOGRAPHY (PET) SCAN to examine the lymphatic network, and specialized immunocytology tests to determine the subtype of lymphoma. Based on the diagnostic findings the oncologist assesses the status of the lymphoma, assigning it a stage classification. Oncologists further designate a grade for non-Hodgkin's lymphoma that characterizes the level of aggressiveness. These assessments determine the appropriate treatment regimens and help valuate the prognosis (likelihood of REMISSION and survival).

Treatment Options and Outlook

Treatment regimens depend on the subtype, stage, and for non-Hodgkin's lymphomas the grade of the cancer as well as the person's age and overall health status. The typical treatment approaches, often administered in combinations, include

LYMPHOMA STAGING (HODGKIN'S AND NON-HODGKIN'S)

Stage	Characteristics
stage 1	early disease involves only a single LYMPH NODE region
stage 2	locally advanced disease involves two or more lymph node regions on one side of the DIAPHRAGM
stage 3	advanced disease involves two or more lymph node regions on both sides of the diaphragm
stage 4	widely disseminated disease involves multiple lymph node regions and METASTASIS to other organs such as the BONE or BRAIN
A	no symptoms at time of diagnosis (asymptomatic)
B	symptoms present at time of diagnosis
E	lymphoma is present in an organ outside the lymphatic system with no lymph node involvement

- RADIATION THERAPY, either above the diaphragm only (mantle field radiation) or from the neck to the pelvis (total nodal irradiation)
- CHEMOTHERAPY
- IMMUNOTHERAPY, also called biological response modifier therapy, including monoclonal antibody (MAb) therapy
- BONE MARROW TRANSPLANTATION and peripheral blood stem cell transplantation (PBSCT)
- watchful waiting for indolent (slow-growing and asymptomatic) lymphomas

Treatment results in at least one remission for most kinds of lymphoma. Many people experience extended remissions with few recurrences, and some people experience such long-term remissions as to have the oncologist consider the lymphoma cured. Other lymphomas are more resistant to treatment. Some chemotherapy drugs are effective as single agents, though more commonly oncologists prescribe chemotherapy drugs in combinations that target specific types of lymphoma. Many treatment regimens are cycles that repeat over several months to a year. Numerous complications resulting from treatment may occur, and vary with the treatment regimen, type and stage of lymphoma, and person's age and general health status.

CHEMOTHERAPY DRUGS USED TO TREAT LYMPHOMA

5-fluorouracil	bleomycin
carmustine	chlorambucil
cisplatin	cyclophosphamide
cytarabine	dexamethasone
doxorubicin	etoposide
fludarabine	fluoxymesterone
hydroxydaunomycin	ifosfamide
melphalan	methotrexate
mitoxantrone	pentostatin
prednisone	prednisone
procarbazine	rituximab
tositumomab	vincristine

Risk Factors and Preventive Measures

Researchers do not know what causes lymphoma, though a number of environmental factors appear to increase the risk for developing these forms of cancer. The most significant risk is for people who receive IMMUNOSUPPRESSIVE THERAPY after ORGAN TRANSPLANTATION, who are 100 times more likely to develop non-Hodgkin's lymphoma. Other suspected risk factors include

- HIV/AIDS
- INFECTION with human T-lymphocytic virus 1 (HTLV-1), EPSTEIN-BARR VIRUS, or human herpesvirus 8 (HHV-8)
- infection with *HELICOBACTER PYLORI*, the BACTERIA believed responsible for STOMACH CANCER
- occupational exposure to benzene
- occupational exposure to agricultural pesticides and herbicides, notably organophosphates and chlorophenols
- first-degree relatives (parents, siblings, children) who have lymphoma
- chromosomal TRANSLOCATION and other abnormalities

However, researchers do not know the extent to which these factors influence the development of lymphoma. Many people who develop lymphoma have no history of exposure to these factors, and far more people than not who have exposure do not develop lymphoma. Reducing or eliminating exposure to environmental toxins, treating infections such as *H. pylori,* and maintaining nutritious EATING HABITS can improve health overall. Otherwise, there are no known measures to prevent lymphoma.

See also AMYLOIDOSIS; B-CELL LYMPHOCYTE; CANCER RISK FACTORS; CANCER TREATMENT OPTIONS AND DECISIONS; ENVIRONMENTAL HAZARD EXPOSURE; ERYTHROPOIETIN (EPO); LEUKEMIA; LIFESTYLE AND HEALTH; MULTIPLE MYELOMA; NATURAL KILLER (NK) CELL; SIGNS AND SYMPTOMS OF CANCER; SMOKING AND HEALTH; STAGING AND GRADING OF CANCER.

lymph vessels An extensive network of channels that collect and circulate LYMPH, a watery fluid containing immune cells and substances as well as pathogens cleansed from the BLOOD and tissues. The lymph vessels, also called lymphatics, are similar in structure to the capillaries and veins of the cardiovascular system but have thinner walls. The lymph vessels carry lymph from the tissues through the lymph nodes, where lymphocytes neutralize or kill and macrophages consume pathogens, then deliver the cleansed fluid to the blood.

The smallest of the lymph vessels are the lymphatic capillaries, which arise from cul-de-sac structures within the interstitial fluid (fluid between the cells) in the tissues surrounding the CAPILLARY BEDS of the cardiovascular system. The shingled, single-cell walls of the lymphatic capillaries are permeable, allowing fluid to seep inside though preventing it from seeping back out. The lymphatic capillaries merge into the afferent lymphatics, somewhat larger lymph vessels that carry the lymph among the lymph nodes. The lymphatic capillaries in the SMALL INTESTINE, called lacteals, are uniquely able to absorb the fatty products of digestion, which they ultimately deliver to the blood.

The larger lymph vessels are not permeable and contain valves to keep lymph moving in only one direction, toward the central body. Their pathways roughly parallel those of the cardiovascular circulatory structures. In the central trunk region the lymph vessels merge into three reservoir-like structures. These structures are the

- CISTERNA CHYLI, which collects lymph from the lacteals and the abdominal lymph vessels
- THORACIC DUCT, which collects lymph from the cisterna chyli and the upper left body
- RIGHT LYMPHATIC DUCT, which collects lymph from the upper right body and head

The thoracic duct parallels the AORTA and drains into the left subclavian vein. The right lymphatic duct drains into the right subclavian vein. The lymph then becomes part of the blood.

For further discussion of lymph vessels within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also LYMPHADENITIS; LYMPHEDEMA; LYMPH NODE; SENTINEL LYMPH NODE DISSECTION.

M–N

megakaryocyte See BONE MARROW.

methemoglobinemia A BLOOD oxygenation disorder in which methemoglobin, a structure of HEMOGLOBIN molecules that prevents iron from binding with oxygen, accumulates in the BLOOD. The result is diminished or insufficient oxygen delivery to the body's cells. Methemoglobin represents excessive iron molecule structures that are in a ferric state, in which they are unable to bind with oxygen. Normal iron molecules in the hemoglobin are ferrous. Methemoglobin forms naturally in the blood as a process of oxidation (cellular METABOLISM), though an enzyme system that converts ferric iron to ferrous iron continuously restores methemoglobin to hemoglobin. Methemoglobin is normally present in the blood in minute quantities, accounting for less than 1 percent of the total hemoglobin forms. Levels above 10 percent begin to cause symptoms, and levels above 70 percent are fatal.

A potential cause of methemoglobinemia is the illicit use of "nitrite poppers," inhaled isobutyl nitrite, butyl nitrite, and amyl nitrate products that are popular among some recreational DRUG users.

Methemoglobinemia most commonly results from toxic exposure to oxidizing chemicals or drugs. Dozens of industrial chemicals can cause methemoglobinemia, as can numerous medications in the nitrate, chlorate, and sulfonamide families of drugs, as well as topical anesthetics such as benzocaine and lidocaine. Exposure is usually chronic. Other causes of methemoglobinemia include hemoglobin disorders that allow excessive methemoglobin formulation and abnormalities in the blood enzyme system that normally removes methemoglobin from the blood.

Symptoms and Diagnostic Path

Symptoms of methemoglobinemia may mimic those of ANEMIA, such as fatigue and shortness of breath (DYSPNEA) especially with exertion or exercise, though important differences are present to help distinguish methemoglobinemia from other hemoglobin disorders. The most significant is a characteristic CYANOSIS that gives the SKIN a bluish brown color and does not improve with the administration of OXYGEN THERAPY. Blood tests that analyze hemoglobin composition determine the amount of methemoglobinemia in the blood; levels higher than 1 or 2 percent confirm the diagnosis though most people who show symptoms have much higher levels.

Treatment Options and Outlook

Most often, removing exposure to the causative substance allows the blood to recover on its own, usually within 72 hours. The doctor may choose to hospitalize the person until hemoglobin levels return to normal, to make sure the person receives adequate oxygenation. When symptoms are severe or persist, treatment may include methylene blue, a chemical that converts the hemoglobin's iron from ferric to ferrous. The typical therapeutic approach is to administer an intravenous injection of methylene blue to rapidly convert enough methemoglobin to hemoglobin to relieve symptoms, then switch to oral methylene blue until hemoglobin returns to normal. Rarely, a person who is having severe symptoms may require hyperbaric treatment, in which oxygen under pressure can enter the body through the skin to deliver oxygen to the tissues. Hyperbaric

therapy may also be appropriate for people who cannot take methylene blue.

Recovery is generally complete when the cause is toxic exposure. Genetic disorders of the hemoglobin or the enzyme mechanisms that regulate the balance between methemoglobin and hemoglobin may result in chronic methemoglobinemia and consequently the need for ongoing treatment (such as oral methylene blue) to prevent toxic accumulations.

Risk Factors and Preventive Measures

The most common cause of methemoglobinemia is toxic exposure to substances that cause oxidation, which overwhelms the body's normal mechanisms for managing cell metabolism. Avoiding chemicals, including drugs, that may cause methemoglobinemia is not simple, as they number in the dozens and include such commonly used medications as nitrates (cardiovascular) and topical anesthetics. People who have genetic disorders that interfere with hemoglobin production and function have increased risk for methemoglobinemia and should make every effort to avoid known causative agents.

See also ENVIRONMENTAL HAZARD EXPOSURE; G6PD DEFICIENCY; OCCUPATIONAL HEALTH AND SAFETY; OXYGEN–CARBON DIOXIDE EXCHANGE; SICKLE CELL DISEASE.

monocyte A LEUKOCYTE (white BLOOD cell), also called an agranulocyte, that has a single-lobed nucleus and contains no granules in its cytoplasm. The BONE MARROW and the LYMPH nodes produce monocytes, which have a two-phase existence in the body. During the first phase, the monocyte circulates in the blood and the lymph, functioning as a PHAGOCYTE that consumes pathogenic particles in the circulation. After about 24 hours the monocyte migrates into the tissue to enter its second phase of life. Once in the tissue the monocyte matures, becoming a fixed phagocytic cell called a macrophage that may acquire a specific name, depending on its location. About half of the body's macrophages migrate to the lymphatic structures. Most of the remainder reside in the LIVER, where they are called Kupffer cells. Macrophages that settle in the layers of the SKIN are Langerhans cells, and those that inhabit the BONE are osteoclasts.

Two to 8 percent of the body's leukocytes are monocytes; a normal monocyte count is 200 to 1100 monocytes per microliter of whole blood. The number of monocytes in circulation may increase with INFECTION, LEUKEMIA, LYMPHOMA, many other types of cancer, and AUTOIMMUNE DISORDERS in which there is active INFLAMMATION and autoimmune activity. The number of monocytes in circulation may decrease in aplastic ANEMIA and with steroid medications.

For further discussion of monocytes within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also CELL STRUCTURE AND FUNCTION; ERYTHROCYTE; GRANULOCYTE; HEMATOPOIESIS; SKIN-ASSOCIATED LYMPHOID TISSUE (SALT).

multiple myeloma A CANCER of the BONE MARROW in which PLASMA cells, also called myeloma cells or myelocytes, proliferate, accumulating as lesions (growths) to develop within the BONE marrow cavities of the bones. The lesions prevent normal functioning of the bone marrow. They also damage bone tissue and weaken the bone structure. Plasma cells derive from lymphocytes that migrate to the bone marrow. Their function is to produce immune antibodies, or immunoglobulins, that are essential for the body's IMMUNE RESPONSE. They generally make up less than 5 percent of the cells in the bone marrow. In multiple myeloma plasma cells make up 10 percent or more of the bone marrow's cells. The cancerous plasma cells of multiple myeloma overproduce certain immune antibodies called monoclonal proteins or M-proteins. M-proteins alter the ways in which immunoglobulins bind with B-cell lymphocytes in the blood, reducing their ability to fight INFECTION.

The M-proteins also activate specialized phagocytic cells in the bone, called osteoclasts, accelerating the deconstruction phase of bone remodeling (the process through which bone tissue continuously replenishes). Osteoclastic activity releases excessive calcium into the bloodstream, affecting numerous body systems, including cardiovascular function and renal (kidney) function. The KIDNEYS produce ERYTHROPOIETIN (EPO), the HORMONE that stimulates the bone marrow to produce erythrocytes (red blood cells). Damage to the kidneys

such as occurs with multiple myeloma reduces EPO production, resulting in moderate to significant ANEMIA. M-proteins can bind with erythrocytes in the blood, further reducing their ability to transport oxygen. M-proteins can also bind with other substances in the blood including hormones and cells such as platelets. M-protein binding with platelets results in COAGULATION (clotting) abnormalities including excessive bleeding or thrombosis (clot formation within the blood vessels).

In the late 1990s researchers achieved a significant breakthrough in identifying the possible causes of multiple myeloma with the discovery of a connection between multiple myeloma and certain infections, notably herpesvirus type 8 (which causes another cancer, KAPOSI'S SARCOMA) and HEPATITIS C. As well, doctors have long noted connections between multiple myeloma and occupational exposure to pesticides (notably DDT) and petroleum products, and to radiation exposure such as RADIATION THERAPY. Multiple myeloma is more common in people over age 55 and accounts for 1 percent of all cancers doctors diagnose in the United States each year. It is more common in men than women and affects twice as many African Americans, though researchers are unsure of the reasons.

Symptoms and Diagnostic Path

About half of people diagnosed with multiple myeloma have no symptoms at the time of diagnosis, when blood tests performed for other reasons reveal the abnormalities consistent with multiple myeloma. Blood tests early in the course of the cancer may produce inconsistent and nonspecific findings that become relevant with subsequent diagnostic procedures. When symptoms are present they may include

- fatigue, especially with exertion
- frequent nosebleeds (EPISTAXIS) or easy bruising
- GASTROINTESTINAL BLEEDING
- PAIN, often in the back or that feels as though it originates in the bones
- excessive thirst
- HEADACHE
- a haze over the field of vision

Diagnostic blood tests typically show elevated blood calcium levels, altered blood cell counts, increased blood proteins, increased blood volume, the presence of M-proteins, and the presence of myelocytes (PLASMA cells) in the blood circulation. NEUTROPENIA and anemia are often present. Diagnostic imaging such as X-rays, COMPUTED TOMOGRAPHY (CT) SCAN, POSITRON EMISSION TOMOGRAPHY (PET) SCAN, and MAGNETIC RESONANCE IMAGING (MRI) allow the oncologist to assess the extent of bone involvement and damage. Bone marrow biopsy reveals high plasma cell counts and abnormal bone marrow structure.

Treatment Options and Outlook

CHEMOTHERAPY is the treatment of choice for multiple myeloma. The first chemotherapy agent developed to treat multiple myeloma in 1958, melphalan, remains the first line DRUG of choice today, commonly given in combination with prednisone, a corticosteroid medication. Oncologists use other chemotherapy agents, usually in combinations with each other and with CORTICOSTEROID MEDICATIONS, to tailor treatment regimens to an individual's age and the cancer's presentation, other health considerations, and preferences. Initial treatment typically produces REMISSION, though RECURRENCE within two years is common. Some people benefit from radiation therapy that targets myeloma lesions within the bones. New treatments continue to emerge as researchers gain understanding of the mechanisms of multiple myeloma.

DRUGS USED TO TREAT MULTIPLE MYELOMA

bortezomib	busulfan
carmusine	cisplatin
cyclophosphamide	dexamethasone
doxorubicin	etoposide
melphalan	prednisone
thalidomide	vincristine

Thalidomide and thalidomide analogs Thalidomide, which debuted in the 1950s as a treatment for MORNING SICKNESS and insomnia in PREGNANCY and quickly gained notoriety for causing BIRTH DEFECTS, emerged in the late 1990s as a successful treatment in some people for multiple myeloma that resists other therapies. Thalidomide sup-

presses the maturation of lymphocytes to plasma cells. Thalidomide analogs (such as Revimid and Actimid) are drugs closely related in chemical structure to thalidomide. Oncologists may administer thalidomide in combination with prednisone or dexamethasone, corticosteroid medications that help suppress bone marrow activity to slow the production of cancerous plasma cells.

Proteasome inhibitors In 2003 the US Food and Drug Administration (FDA) approved the proteasome inhibitor bortezomib (Velcade) for people who have experienced two relapses following conventional treatment approaches. Proteasome inhibitors block the actions of enzymes within cells that are crucial to the cell's ability to divide (reproduce). Clinical studies continue to investigate the effectiveness of these drugs, which appear to cause fewer side effects than conventional chemotherapy, as first-choice treatment.

Bone marrow and stem cell transplantation Autologous BONE MARROW TRANSPLANTATION or STEM CELL transplantation (self-transplantation with harvested cells), achieves remission in many people. For autologous transplantation, the oncologist harvests peripheral BLOOD STEM CELLS (PBSC) or stem cells from healthy areas of bone marrow; administers high-DOSE chemotherapy after cell harvesting to kill the cancerous bone marrow; and administers the harvested bone marrow or stem cells, which then grow to replace the cancerous bone marrow. Allogeneic stem cell transplantation, which uses stem cells from a tissue-matched donor, carries relatively high risks of complications including transplant rejection, infection, and other reactions, but is so far the only hope for a cure of multiple myeloma. Nonmyeloablative (the patient's bone marrow is not destroyed) allogeneic stem cell transplantation reduces the high risks of high-dose chemotherapy. Though not curative it may offer increased survival time.

Adjunctive therapies Oncologists use various medications to mediate the side effects of treatment as well as the complications that arise as the course of the cancer progresses. Among them are:

- Statins (such as Lipitor and Mevacor) counters the osteoclastic (bone destruction) stimulation M-proteins generate. Researchers discovered in the early 2000s that the statin medications used to treat HYPERLIPIDEMIA (elevated blood cholesterol and blood lipid levels) additionally stimulate osteoblastic (bone construction) activity, resulting in increased production of new bone tissue.
- Therapeutic EPO supplementation (Procrit) stimulates bone marrow production of erythrocytes, relieving anemia.
- Bisphosphonates bind to damaged bone cells and so prevent further osteoclastic action (destruction). This allows the body's natural bone remodeling mechanisms to repair the damage and rebuild the bone. However, bisphosphonates present the potential for serious kidney damage.
- ANTIBIOTIC MEDICATIONS aggressively treat the infections that become increasingly common as dysfunction of the IMMUNE SYSTEM progresses.

Lifestyle factors Because multiple myeloma affects bone remodeling, daily weight-bearing exercise such as walking is important to stimulate the body's normal osteoblastic (bone-constructing) mechanisms. These mechanisms further help bone tissue retain calcium, reducing the amounts of calcium that leaches into the circulation. Drinking lots of water to maintain high HYDRATION is also especially important. Staying well hydrated helps offset the tendency of the blood to become hyperviscous (thickened) as a consequence of the changes in its constitution that take place with the multiple myeloma. It also helps protect the kidneys by lowering the concentration of calcium and M-proteins that they must filter from the blood and pass in the URINE. Nutritious EATING HABITS provide the body with the NUTRIENTS it needs to maintain the best health status possible.

Risk Factors and Preventive Measures

Though environmental exposure, notably to pesticides and radiation, appears to play a role in the development of multiple myeloma, researchers do not know the mechanisms of such exposure. Many people who develop multiple myeloma do not have a known history of exposure to substances so far linked with an increased risk for this form of cancer, making it difficult for health

experts to recommend effective preventive measures.

Potential complications of both the multiple myeloma and its treatments present risks that affect the course of the cancer as well as the prognosis (outlook). M-proteins bind with numerous cell types, causing deposits to accumulate. Such deposits on NERVE cells tend to cause NEUROPATHY (pain or insensitivity). Such deposits within organs, such as the LIVER and the kidneys, may adversely affect their functions. Kidney damage may result in kidney failure and the need for dialysis. As well, chemotherapy agents and high-dose corticosteroids, standards of treatment for multiple myeloma, present the potential for numerous adverse effects. Most people who have multiple myeloma experience several periods of remission ranging from six months to two years in duration with each course of treatment.

See also AMYLOIDOSIS; CANCER TREATMENT OPTIONS AND DECISIONS; IMMUNOGLOBULIN; LEUKEMIA; LYMPHOMA.

myelocyte See BONE MARROW.

myelodysplasia syndrome Different constellations of symptoms, all arising from dysfunction of the BONE MARROW and all leading to various cytopenias (low BLOOD cell counts). In myelodysplasia, also called preleukemia, the number of hematopoietic cells within the BONE marrow increases but the produced cells are disordered and often released to the BLOOD while they are immature. Myelodysplasia syndrome most commonly affects people over age 60. Doctors do not know what causes this syndrome though a significant percentage of people who develop myelodysplasia have had exposure to industrial chemicals (notably benzenes) or radiation. Children who develop myelodysplasia often have underlying genetic disorders such as DOWN SYNDROME.

Myelodysplasia may affect any of the blood cells, resulting in a sometimes confusing clinical picture of mixed symptoms such as bleeding (PLATELET involvement) in combination with ANEMIA (ERYTHROCYTE involvement) or with frequent infections (LEUKOCYTE involvement). The SPLEEN often becomes enlarged (SPLENOMEGALY) as it attempts to filter defective blood cells from the blood and activate its hematopoietic functions to increase blood cell production in compensation for the bone marrow's inability to meet the body's needs. In some people myelodysplasia syndrome progresses to chronic or acute LEUKEMIA. Examination of the blood cells in a blood sample and bone marrow biopsy allow the doctor to make the diagnosis. Treatment may include transfusions of the deficient blood components and ANTIBIOTIC MEDICATIONS as necessary to treat infections. The outlook depends primarily on the type of blood cells involved.

See also BLOOD TRANSFUSION; ENVIRONMENTAL HAZARD EXPOSURE; HEMATOPOIESIS; INFECTION; LYMPHOMA.

myelofibrosis A chronic, degenerative condition of the BONE MARROW in which fibrous tissue replaces the red BONE marrow. Researchers do not know what causes myelofibrosis, which typically develops in people between the ages of 50 and 70, but believe it is an autoimmune response from a single defective blood STEM CELL (called a clonal dysfunction). The IMMUNE SYSTEM fails to recognize the deformed cells and produces antibodies to attack them. Because all BLOOD cells originate from BLOOD STEM CELLS, the attacking antibodies cause extensive damage within the bone marrow. The body's efforts to repair this damage result in pervasive SCAR formation that progressively shuts down the bone marrow.

The most apparent consequence is severe ANEMIA, as 99 percent of the bone marrow's production is oxygen-bearing erythrocytes (red blood cells). The shortfall activates the body's reserve erythropoietic functions in the LIVER and the SPLEEN, which begin producing erythrocytes. However, these organs cannot meet the demand and so both begin to enlarge with the effort (HEPATOMEGALY and SPLENOMEGALY, respectively).

Symptoms of myelofibrosis include those of anemia as well as bone PAIN, easy bleeding, and low resistance to infection as a consequence of diminished LEUKOCYTE (white blood cell) production. Blood tests show a low ERYTHROCYTE count, often low leukocyte and PLATELET counts, and characteristic "tear drop" deformity of the erythrocytes. Bone marrow biopsy shows the infiltration of fibrous tissue.

Treatment targets boosting the blood's erythrocytes by BLOOD TRANSFUSION and ERYTHROPOIETIN (EPO)

supplementation to stimulate the remaining red bone marrow to increase its erythrocyte production (erythropoiesis). Occasionally CHEMOTHERAPY and RADIATION THERAPY to suppress bone marrow function, curtailing proliferation of the defective stem cells, slows the condition's progression. BONE MARROW TRANSPLANTATION is sometimes a viable option. The outlook for myelofibrosis is variable; treatment is not curative and ultimately the bone marrow fails completely. Occasionally myelofibrosis evolves into acute myeloid LEUKEMIA, a rapidly progressive type of cancer in which blast cells (immature leukocytes) take over the bone marrow.

See also POLYCYTHEMIA VERA; THROMBOCYTHEMIA; THROMBOCYTOPENIA.

neutropenia Lower than normal numbers of neutrophils circulating in the BLOOD. Neutrophils are the most abundant of the three subtypes of granulocytes; the GRANULOCYTE is a type of LEUKOCYTE (white blood cell). Neutropenia, which can be acute or chronic, results in increased susceptibility to bacterial and fungal (yeast) INFECTION. Severe neutropenia can leave the body virtually defenseless against such infection, as neutrophils are the front line of response to invading pathogenic microorganisms.

The causes of neutropenia are numerous. Among the most common are

- acute viral infections such as mononucleosis, CYTOMEGALOVIRUS (CMV), INFLUENZA, HIV/AIDS, and HEPATITIS
- AUTOIMMUNE DISORDERS
- cancers of the BONE MARROW such as LEUKEMIA and MULTIPLE MYELOMA
- LYMPHOMA
- Vitamin B_{12} deficiency
- long-term, chronic ALCOHOL consumption
- RADIATION THERAPY and CHEMOTHERAPY
- adverse DRUG reactions, notably with NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and penicillin ANTIBIOTIC MEDICATIONS

Chronic neutropenia is common with chronic infections such as HIV/AIDS and with AUTOIMMUNE DISORDERS. The primary symptoms of neutropenia are typically those of the infection that is present. Diagnostic blood tests that show lowered numbers of neutropenia in the blood confirm the diagnosis. Treatment targets the underlying health condition or removes the offending medication. In many people neutropenia is transient and self-limiting.

See also LEUKOPENIA; LYMPHOCYTOPENIA; MONONUCLEOSIS; INFECTIONS; THROMBOCYTOPENIA.

neutrophil See GRANULOCYTE.

P

phagocyte A white BLOOD cell (LEUKOCYTE) that consumes pathogens during an IMMUNE RESPONSE called PHAGOCYTOSIS. Granulocytes, and in particular neutrophils, are the primary phagocytes in the circulating blood. Macrophages are phagocytes that reside primarily in the LYMPH structures and the tissues. Protein markers on the surface of the PATHOGEN, called opsonins, attract phagocytes to the pathogen's location. The phagocyte extends its wall to encircle the pathogen, then releases enzymes that digest the pathogen. An individual phagocyte may digest up to a dozen pathogenic particles during the course of its existence.

See also BACTERIA; CELL STRUCTURE AND FUNCTION; MONONUCLEAR PHAGOCYTE SYSTEM.

phagocytosis The process through which a PHAGOCYTE (a specialized LEUKOCYTE) consumes a PATHOGEN or other cellular particle. Phagocytosis is a key defense mechanism of the body's IMMUNE RESPONSE and may take place in the BLOOD, primarily the domain of granulocytes (neutrophils and eosinophils), and in the tissues, primarily the realm of tissue-based monocytes (macrophages). When a pathogen invades the body, the immune response sends substances called opsonins to coat its surface. This process, called opsonization, marks the pathogen, attracting phagocytes. The most common opsonins are antibodies and the proteins the complement system produces.

The blood and the LYMPH carry phagocytes to the sites of opsonized pathogens. When the phagocyte reaches the pathogen it extends its cell wall to enclose the pathogen within its cytoplasm. Once enclosure is complete the phagocyte releases enzymes called lysozymes that digest the pathogen, breaking it down into its molecular components which the cell then recycles or releases as metabolic waste. The primary blood-based phagocytes are neutrophils, which respond to pathogens, and eosinophils, which respond to antigens. Monocytes circulate in the blood only for about 12 hours and then migrate into the tissues. Specialized phagocytes in the LIVER, the Kupffer cells, function in a somewhat cannibalistic manner, cleansing expired granulocytes from the circulating blood and recycling their molecular components into the bloodstream for other uses.

See also MONONUCLEAR PHAGOCYTE SYSTEM.

phlebotomy The clinical term for puncturing a VEIN with a sterile needle to withdraw BLOOD. Phlebotomy may be diagnostic, such as when drawing blood for diagnostic blood tests, or therapeutic, such as a treatment for HEMOCHROMATOSIS. Phlebotomy may be mildly uncomfortable, as the needle may sting as it penetrates the SKIN and the vein. The blood withdrawal itself is painless. The risks of phlebotomy are minor for most people and include mild bleeding, bruising, and discomfort at the puncture site.

See also BLOOD DONATION.

plasma The liquid portion of the BLOOD. Plasma is about 90 percent water and makes up 55 percent of the total blood volume. It contains numerous substances dissolved in it including electrolytes, hormones, enzymes, antibodies, GLUCOSE, and CLOTTING FACTORS (specialized proteins). It also carries the blood cells in suspension. Plasma is available for transfusion as a blood product, in fresh or fresh-frozen form. Plasma derivative products extracted from donated plasma include cryoprecipitated antihemophilic factor (AHF), ALBUMIN, IMMUNOGLOBULIN, and Rh immunoglobulin.

For further discussion of the plasma within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also BLOOD TRANSFUSION; ERYTHROCYTE; HEMAPHERESIS; HORMONE; LEUKOCYTE; LYMPHOCYTE; MONOCYTE.

plasmapheresis See HEMAPHERESIS.

platelet The cellular structure indispensable for COAGULATION (clotting), also called a thrombocyte. Platelets, which are actually cell fragments rather than intact cells, separate from parent cells in the BONE MARROW called megakaryocytes, the largest cells in the BONE marrow. When platelets emerge into the circulation they become the smallest cell particles in the circulating blood. Their small size permits them to travel into any blood vessel, even the tiniest arterioles and venules, to respond to bleeding. Platelets lack nuclei and thus, like erythrocytes, cannot divide. They live in the circulation for about 10 days.

The normal number of platelets in the blood is 130,000 to 400,000 per cubic milliliter. The SPLEEN holds about 30 percent of the blood's platelets within its red pulp, releasing them into the circulation when needed to respond to bleeding. This containment helps reduce the risk for inadvertent agglutination as platelets swirl into contact with one another in the bloodstream.

Any breach in a blood vessel that allows blood to escape results in the release of the enzyme tissue factor (factor III), which attracts droves of platelets to the site. As the platelets agglutinate (come into contact with the damaged site and with one another) they release chemicals such as serotonin, thromboxane, and phospholipids that extend and focus the coagulation cascade.

For further discussion of platelets within the context of blood and lymph structure and function, please see the overview section "The Blood and Lymph."

See also ANTICOAGULATION THERAPY; ARTERY; CELL STRUCTURE AND FUNCTION; CLOTTING FACTORS; HEMAPHERESIS; VEIN.

platelet aggregation The process through which platelets respond to chemical signals in the BLOOD, allowing them to adhere to each other and to collagen fibers in the blood to form the hemostatic plug that will become a blood clot at the conclusion of the COAGULATION cascade. The formation of collagen and the conversion of fibrinogen (clotting factor I) to the enzyme fibrin together initiate a sequence of chemical conversions that alter PLATELET surface proteins as well as attract more platelets to the location of the injury. As the coagulation cascade continues, platelets accumulate. The platelets change shape, developing threadlike extensions called pseudopods that allow them to extend like vines into the weave of collagen fibers. The surface of the platelets continues to undergo chemical changes that attract fibrinogen and release arachidonic acid, which oxidizes to form PROSTAGLANDINS, short-acting hormones that are key players in the IMMUNE SYSTEM'S INFLAMMATION response. Prostaglandins further attract platelets to the site.

Converted CLOTTING FACTORS begin to weave fibers of protein among the fibers of fibrin, thrombin, and collagen, forming a netlike structure that entraps other cells flowing through the blood. When the clot reaches critical mass additional chemical reactions begin to shut down the coagulation cascade, bringing the clotting process to a halt. The surface proteins of circulating platelets revert, and the platelets no longer adhere to each other. The reversion also activates mechanisms within the platelets that cause them to contract, pulling them tightly into the clot structure. Other proteins cause the clot to harden, cementing it in place.

Inflammation of the ARTERY walls, such as occurs with CORONARY ARTERY DISEASE (CAD), attracts platelets in the same manner as do wounds, setting in motion the events of platelet aggregation in ways that are detrimental to health. Doctors often prescribe antiplatelet medications to slow platelet aggregation in people who have had HEART ATTACK OR STROKE, or who have CAD. Most of these medications work by blocking the oxidation of arachidonic acid, which then inhibits prostaglandin formation. The most commonly used antiplatelet medication is aspirin. Platelet aggregation can also occur as a SIDE EFFECT of medications or a dysfunction of coagulation.

See also ANTICOAGULATION THERAPY; ATHEROSCLEROTIC PLAQUE; C-REACTIVE PROTEIN.

polycythemia vera A myeloproliferative condition of the BLOOD in which the red BONE MARROW produces an excessive volume of erythrocytes (red blood cells), platelets, and neutrophils that results in increased cell volume and decreased fluid volume (PLASMA) in the blood. This myeloproliferation (overproduction by the bone marrow) thickens the blood (hyperviscosity), making it more difficult for the cardiovascular system to transport and increasing the risk for thrombosis (blood clots). As the myeloproliferation progresses, the marrow pushes immature, deformed, and defective cells into the blood that are unable to perform the normal functions of their cell types. Polycythemia vera is a chronic and potentially debilitating disorder most commonly diagnosed in people age 60 and older.

Symptoms and Diagnostic Path

Symptoms may not appear until the bone marrow dysfunction is considerably advanced and typically include

- tiredness and fatigue
- weakness
- HEADACHE
- lightheadedness
- easy bleeding or bruising
- PRURITUS (itching)
- SKIN flushing (redness), particularly of the face

The doctor's examination often reveals an enlarged SPLEEN (SPLENOMEGALY), a consequence of the overload on the spleen to remove defective erythrocytes from the circulating blood or to produce additional erythrocytes if those in circulation are too defective to adequately transport oxygen (ANEMIA). Some people also have an enlarged LIVER (HEPATOMEGALY), as the liver too has a role in cleansing dysfunctional erythrocytes from the blood. Diagnostic blood tests characteristically show elevated ERYTHROCYTE, neutrophil, and PLATELET counts, with the hematocrit (percentage of erythrocytes in the blood) greater than 54 percent in men or 49 percent in women. The doctor may also perform a bone marrow biopsy, which demonstrates clusters of megakaryocytes (the parent cells of platelets) and other characteristic alterations in the marrow's structure.

Treatment Options and Outlook

PHLEBOTOMY (therapeutic withdrawal of blood) is adequate treatment for many people who have polycythemia vera, particularly when the diagnosis comes early in the condition. The usual therapeutic approach is daily phlebotomy to remove 300 to 500 milliliters of blood until the hematocrit drops to 45 percent. Weekly to monthly phlebotomy sessions then may keep the condition in check.

When phlebotomy is not sufficient, substances to suppress bone marrow function, called myelosuppressive therapy, can put the condition in REMISSION for up to several years at a time. Myelosuppressive therapy has a high risk for causing acute myeloid LEUKEMIA, however, so current treatment protocols call for its use only in people over age 70.

The most significant and frequent complications of polycythemia vera are thrombosis (the formation of blood clots in the blood vessels), which can lead to HEART ATTACK or STROKE, and acute myeloid leukemia. Without treatment polycythemia vera is generally fatal within two years. With treatment, many people enjoy good QUALITY OF LIFE for 15 to 20 years beyond diagnosis.

Risk Factors and Preventive Measures

Because researchers do not know what causes polycythemia vera, there are no known preventive measures. The condition is uncommon, and more likely to occur in men than women. Polycythemia vera is unusual in a person under age 40. Early diagnosis and treatment improves quality of life and outlook.

See also HEMOCHROMATOSIS; MYELOFIBROSIS; THROMBOCYTHEMIA; THROMBOCYTOPENIA.

R–S

reticulocyte An ERYTHROCYTE (red BLOOD cell) that enters the blood's circulation from the BONE MARROW just before it has reached maturity. Reticulocytes are somewhat larger than erythrocytes and normally make up about 1 percent of the erythrocytes in circulation. A reticulocyte matures into an erythrocyte after being in circulation for about a day. Reticulocytes are still continuing to synthesize (make) HEMOGLOBIN, so contain somewhat less hemoglobin than mature erythrocytes.

An increased number of reticulocytes in circulation indicates the BONE marrow is producing erythrocytes more rapidly than normal. Accelerated erythropoiesis may suggest various underlying causes, such as undetected internal bleeding, hemolytic ANEMIA, and extended exposure to high altitude (which increases the body's need for oxygen). The reticulocyte count also rises in PREGNANCY and with some medications such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), levodopa taken to treat PARKINSON'S DISEASE, and sulfonamide ANTIBIOTIC MEDICATIONS.

A decreased number of reticulocytes in circulation suggests chronic INFECTION, exposure to radiation, aplastic anemia, or iron-deficiency anemia. The reticulocyte count also may drop with CHEMOTHERAPY, the antibiotic chloramphenicol, and the immunosuppressant medication azathioprine typically taken after ORGAN TRANSPLANTATION to prevent organ rejection or severe RHEUMATOID ARTHRITIS.

For further discussion of reticulocytes within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also CELL STRUCTURE AND FUNCTION; HEMATOPOIESIS; IMMUNOSUPPRESSIVE THERAPY.

Rhesus (Rh) blood type See BLOOD TYPE.

right lymphatic duct A major LYMPH VESSEL that collects LYMPH draining from the right upper body and head. The right lymphatic duct is about a quarter-inch in diameter and two inches long, adjacent to the subclavian VEIN beneath the clavicle (collarbone). It empties into the right subclavian vein, delivering lymph to the bloodstream.

For further discussion of the right lymphatic duct within the context of blood and lymph structure and function, please see the overview section "The Blood and Lymph."

See also CISTERNA CHYLI; THORACIC DUCT.

sickle cell disease An inherited genetic disorder of defective HEMOGLOBIN, a protein compound erythrocytes (red blood cells) contain that binds with oxygen. Though the primary effect of sickle cell disease, also called sickle cell ANEMIA, is anemia (insufficient oxygen in the blood), the condition also causes significant PAIN and damage to organs throughout the body. In the United States sickle cell disease is significantly more common in African Americans. Around the world, sickle cell disease is most common among people of African, northern Mediterranean, Indian, and Middle Eastern descent. About 70,000 Americans have sickle cell disease and another 2 million have sickle cell trait. Sickle cell disease is the most common inherited blood disorder.

Sickle cell disease gets its name from the characteristic sickle shape of the erythrocytes. The deformity results from the defective hemoglobin, called hemoglobin S, which the erythrocytes carry. When hemoglobin S releases oxygen during the OXYGEN-CARBON DIOXIDE EXCHANGE, it polymerizes—its structure undergoes molecular changes that cause its molecular weight to increase. This stiff-

ens and hardens the normally flexible erythrocytes, pulling them into a sickle or crescent shape.

The rigidity and inflexibility prevents the erythrocytes from folding and twisting as they pass through the small blood vessels, causing them to create blockages. The blockages cause swelling, pain, and eventually damage to organs and structures throughout the body. People who have sickle cell disease have very high risk for STROKE, HEART ATTACK, acute chest syndrome (blockages in the lungs that cause INFECTION), and loss of vision.

The changes also make the erythrocytes more fragile, and they easily break apart as the flow of blood jostles them around. Sickled erythrocytes die after only about 20 days in the blood circulation, whereas normal erythrocytes live for 90 to 120 days. The shortened lifespan further limits the ability of the blood to transport oxygen, establishing chronic anemia.

ADAPTIVE DEFECT

Researchers believe the gene mutation that causes sickle cell disease originated in the form of sickle cell trait as an adaptation to protect against malaria infection. The sickled erythrocytes resist the parasite that causes MALARIA. In sickle cell trait, the person has some hemoglobin S and mostly normal hemoglobin—an ideal blend for simultaneously maintaining health and thwarting malaria. The adaptation backfires only when two people with sickle cell trait conceive a child, at which time the recessive autosomal inheritance pattern of the mutated hemoglobin gene becomes a risk for passing on too much of a good thing to the child.

The inheritance pattern for sickle cell disease is autosomal recessive, which means both parents must pass the defective hemoglobin gene to their child. People who are carriers of the mutated hemoglobin gene have sickle cell trait, with one mutated and one normal hemoglobin gene. They have small amounts of hemoglobin S though mostly have normal hemoglobin and have no indications of sickle cell disease. However, their children may end up with sickle cell disease if they inherit the sickle cell mutation from each parent. When both parents have sickle cell trait, there is a 1 in 4 chance for the child to have sickle cell disease, a 2 in 4 chance the child will also be a carrier, and a 1 in 4 chance the child will inherit two normal genes.

Symptoms and Diagnostic Path

Symptoms generally begin to emerge when a child is about a year old. For the first year of life the child has an abundant supply of fetal hemoglobin, which has the ability to prevent polymerization of hemoglobin S. However, the child's own hemoglobin gradually replaces the fetal hemoglobin and this protection disappears, typically between age 6 months and 10 months. Early symptoms of sickle cell disease in a child are swollen hands and feet (sometimes called hand and foot syndrome), a consequence of damaged erythrocytes blocking the small blood vessels in the hands and feet to prevent blood from circulating out. Other symptoms include

- pain from blockages
- FEVER
- fatigue from anemia
- diminished vision from damage to the RETINA

People who have sickle cell disease may also have

- frequent infections resulting from damage to the SPLEEN and LYMPH tissues
- jaundice, yellow discoloration of the skin resulting from excessive bilirubin in the blood circulation as the components of the dead erythrocytes accumulate in the LIVER
- delayed growth due to severe anemia

A blood test can detect the presence of hemoglobin S, which affirms the diagnosis. In the United States, hospitals routinely run this test on all newborns. Examination of the erythrocytes under the microscope also shows the characteristic sickle shape.

Treatment Options and Outlook

Treatment for sickle cell disease may include ANALGESIC MEDICATIONS for pain relief, blood transfusions to replace the damaged erythrocytes with healthy erythrocytes (which is effective for the life cycle of the transfused erythrocytes), and the medication hydroxurea (which can reestablish fetal hemoglo-

bin production in some children). BONE MARROW TRANSPLANTATION is sometimes an option for people who have severe symptoms. There is no cure for sickle cell disease. Sickle cell trait does not produce symptoms or develop into sickle cell disease, so it requires no treatment. Many people who have sickle cell trait do not know it.

Risk Factors and Preventive Measures

Because sickle cell disease is an inherited genetic disorder, the only risk factor is heredity. It is a good idea for people who do not know their sickle cell status, especially African Americans, to have the blood test for hemoglobin S before conceiving children. GENETIC COUNSELING can help with family planning decisions when both parents have sickle cell trait.

See also BLOOD TRANSFUSION; HEMOLYSIS; PRIAPISM.

spleen A soft structure of lymphatic tissue located in the upper left abdomen to the left of the STOMACH and PANCREAS, behind the protective enclosure of the rib cage. Fibrous ligaments anchor the spleen to the stomach, COLON, and left kidney. The spleen holds about 300 milliliters of BLOOD, roughly 4 percent of the body's total blood supply, and contains about a third of the body's platelets (the cells responsible for COAGULATION). Its high blood content gives the spleen a dark red color and a somewhat porous texture. The spleen has two main structural and functional sections that filter the blood for different substances, the red pulp and the white pulp.

White Pulp

The white pulp consists of nodules and follicles, similar to those of other lymphatic tissues such as the LYMPH nodes, arranged in sheathlike structures that encase each of the tiny blood vessels (arterioles) within the spleen. The white pulp has two primary roles, to filter antigens from the circulating blood and to produce lymphocytes (a type of LEUKOCYTE). These functions are interrelated in that the lymphocytes bear antibodies specific to the antigens the white pulp traps. When the lymphocytes enter the circulation of the blood or lymph, their antibodies allow them to intercept and destroy pathogens such as viruses or BACTERIA that carry the antigens.

Red Pulp

The red pulp surrounds the white pulp. In the developing fetus the red pulp produces the majority of blood cells, erythrocytes (red blood cells) and leukocytes (white blood cells) alike, until about the fifth month of PREGNANCY, after which the red bone marrow takes over erythropoiesis (ERYTHROCYTE production). Hematopoietic capability of the red pulp remains available but dormant after birth. Throughout life, the red pulp serves as an extramedullary (out of the marrow) resource that the body can press into action to produce erythrocytes.

The red pulp also filters the blood, culling outdated, defective, or damaged erythrocytes from circulation. Phagocytic cells called macrophages that reside within the red pulp break down the erythrocytes, sending components such as HEMOGLOBIN and BILIRUBIN back into the blood for transportation to the LIVER, which recycles them. The red pulp also filters other cellular debris from the blood.

Potential Health Conditions Involving the Spleen

The spleen's primary vulnerability is trauma, which can cause life-threatening hemorrhage (uncontrolled bleeding). A blow to the upper abdomen, such as may occur in MOTOR VEHICLE ACCIDENTS or with aggressive contact sports, can cause a rupture injury to the spleen. Such a blow also can fracture a rib, causing a penetrating wound to the spleen. SPLENECTOMY (surgical removal of the spleen) then becomes necessary. Though not essential for life, the spleen performs numerous functions vital to the IMMUNE RESPONSE and blood cell maintenance. Other lymphatic structures and the liver can partially compensate for the spleen's loss, though the risk for serious INFECTION significantly increases. There are many health conditions that can cause the spleen to enlarge (SPLENOMEGALY). The spleen also enlarges when fighting systemic infections such as infectious mononucleosis and in some cancers.

For further discussion of the spleen within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also CANCER; LYMPH NODE; MONONUCLEAR PHAGOCYTE SYSTEM; MONONUCLEOSIS, INFECTIOUS; PHAGOCYTOSIS.

splenectomy A surgical OPERATION to remove the SPLEEN. Though the spleen performs many vital immune and BLOOD-related functions, it is not essential for life. Because the spleen contains 4 percent of the body's blood volume and a third of its platelets, it is vulnerable to life-threatening hemorrhage with trauma. Doctors may also choose to remove the spleen for therapeutic or prophylactic (preventive) reasons in conditions such as chronic myeloid LEUKEMIA and MYELOFIBROSIS.

Splenectomy may be an OPEN SURGERY or a laparoscopic surgery, depending on the reason and the person's overall health status, performed under general ANESTHESIA. Laparoscopic splenectomy, which involves removing the spleen using a lighted endoscope and small tools the surgeon inserts through four or five small incisions in the upper left abdomen, usually requires an overnight stay in the hospital with three to four weeks for full recuperation. Open splenectomy requires a single incision, four to five inches long, through which the surgeon opens the abdominal cavity and removes the spleen. The open surgery may require three to five days in the hospital with four to six weeks for full recovery.

COMMON REASONS FOR SPLENECTOMY

hemolytic ANEMIA	LEUKEMIA
LYMPHOMA	PORTAL HYPERTENSION
THROMBOCYTOPENIA	trauma with hemorrhage
uncontrolled SPLENOMEGALY	

As with any surgery, excessive bleeding and INFECTION are potential risks. Because absence of the spleen compromises the body's IMMUNE RESPONSE, lowered resistance to infection is a common consequence of splenectomy. Doctors recommend pneumococcal PNEUMONIA vaccination before splenectomy when possible and immediately after when splenectomy is an emergency surgery. The doctor may recommend other immunizations, depending on individual health circumstances. People who have had splenectomy must remain diligent in regard to potential infections, even those that are seemingly minor such as COLDS. Many doctors recommend ANTIBIOTIC PROPHYLAXIS (preventive ANTIBIOTIC MEDICATIONS) to offset the IMMUNE SYSTEM's diminished response.

See also SURGERY BENEFIT AND RISK ASSESSMENT.

splenomegaly An enlarged SPLEEN. Splenomegaly signals an underlying health condition and is not itself a disorder. The spleen is a structure of lymphatic tissue. One of its key roles is to remove old or damaged BLOOD cells from circulation. Many circumstances and health conditions that cause increased numbers of blood cells in the circulation can also cause splenomegaly. These range from systemic infections, such as infectious mononucleosis, to blood disorders, such as THROMBOCYTHEMIA, to cancers, such as LEUKEMIA and LYMPHOMA. Some people feel a sense of uncomfortable fullness with splenomegaly, though most people are unaware of the condition until a doctor detects it.

There is no specific treatment for splenomegaly; so treatment targets the underlying cause. Splenomegaly significant enough to extend the spleen beyond the protective boundary of the rib cage presents a risk for injury resulting in hemorrhage, as the spleen contains about 4 percent of the body's total blood volume and a third of its platelets (the cells responsible for clotting).

CONDITIONS IN WHICH SPLENOMEGALY MAY OCCUR

AMYLOIDOSIS	ANEMIA
CIRRHOSIS	congestive HEART FAILURE
HEPATITIS	leishmaniasis
LEUKEMIA	LEUKOPENIA
LYMPHOMA	MALARIA
MONONUCLEOSIS, INFECTIOUS	MULTIPLE MYELOMA
MYELOFIBROSIS	POLYCYTHEMIA VERA
PORTAL HYPERTENSION	psittacosis
SARCOIDOSIS	SICKLE CELL DISEASE
SYPHILIS	SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
THALASSEMIA	THROMBOCYTHEMIA
THROMBOCYTOPENIA	TUBERCULOSIS

See also HEPATOMEGALY; SPLENECTOMY.

thalassemia A genetic disorder of the BLOOD in which the body fails to produce one or more of the proteins necessary for the synthesis of HEMOGLOBIN, the protein that enables erythrocytes (red blood cells) to carry oxygen. The consequence is ANEMIA (inadequate oxygen to the cells throughout the body). There are two basic types of thalassemia: alpha and beta, designated according to the responsible defunct protein chain. Within these types are a number of subtypes. In general, thalassemia is more common among people of Asian and African heritage (alpha thalassemia) or Mediterranean heritage (beta thalassemia).

Symptoms and Diagnostic Path

Mild thalassemia may produce no symptoms, while severe thalassemia can be life-threatening. Symptoms are generally similar for the major forms of thalassemia and are those of anemia. They may include

- chronic fatigue
- weakness
- HEADACHE
- Shortness of breath, especially with exertion or exercise
- PALPITATIONS

Severe symptoms may involve cardiovascular crisis such as HEART ATTACK. Some forms of thalassemia include excessive iron absorption by the LIVER, HEART, and other organs, resulting in permanent damage such as CIRRHOSIS, LIVER FAILURE, and HEART FAILURE. Long-term thalassemia often results in significant SPLENOMEGALY (enlarged SPLEEN) and permanent changes in BONE structure that weaken the bones (notably with beta thalassemia). In some people the bone changes cause pathologic or spontaneous FRACTURE, which is the first indication of an underlying thalassemia.

The diagnostic path includes blood tests to measure serum iron levels, which are characteristically elevated in severe thalassemia but may be low in mild forms, and to assess hemoglobin composition by hemoglobin electrophoresis. BONE MARROW biopsy demonstrates the altered appearance of developing erythrocytes that characterizes thalassemia. X-rays can confirm changes to the structure of the bones, which are most apparent in the skull and the long bones of the arms and legs.

Treatment Options and Outlook

People who have symptoms as a result of their thalassemia require lifelong BLOOD TRANSFUSION, with either whole blood or packed red cells (erythrocytes), typically every two or three weeks. These transfusions provide normal erythrocytes that can transport oxygen through the bloodstream, with transfusions timed at intervals that approximate the body's normal process of new ERYTHROCYTE release and old erythrocyte cleansing. However, blood transfusions contribute to an escalation of iron accumulation that requires treatment, usually therapeutic CHELATION THERAPY (heavy metals detoxification).

Therapeutic SPLENECTOMY (removal of the spleen) can reduce symptoms when excessive HEMOLYSIS (acceleration of the body's normal process for destroying erythrocytes) contributes to symptoms by stimulating increased erythropoiesis (production of new erythrocytes). BONE MARROW TRANSPLANTATION may become a viable option when other treatment approaches fail to control symptoms and symptoms are severe.

Thalassemia is lifelong. Most people with alpha forms of thalassemia enjoy a good QUALITY OF LIFE,

aside from the intrusion of regular blood transfusions, and normal LIFE EXPECTANCY. Beta forms of thalassemia tend to be more severe and have a less optimistic outlook. The secondary HEMOCHROMATOSIS (iron accumulations in the tissues) can become a significant health factor itself, creating a therapeutic dilemma.

Risk Factors and Preventive Measures

Because thalassemia is genetic and inherited, the primary risk factors are family history and presence of the causative GENE mutations. Doctors advise GENETIC TESTING and GENETIC COUNSELING for people who have family history of thalassemia. It is possible for an individual to carry the gene defect and show no symptoms of the condition, which can result in passing the gene defect, and the disease, to the individual's children.

See also HEMATOPOIESIS; INHERITANCE PATTERNS; MUTATION; SICKLE CELL DISEASE.

thoracic duct The largest vessel of the lymphatic system. The thoracic duct collects LYMPH from the CISTERNA CHYLI and the left upper body, and drains into the left subclavian VEIN to deliver lymph to the bloodstream. About the diameter of a pencil, the thoracic duct extends from the cisterna chyli in the central trunk to base of the neck, a distance of about 16 inches, somewhat paralleling the AORTA. Like a vein, the thoracic duct has smooth-MUSCLE walls that rhythmically contract and contains valves to prevent its contents from backflowing. Muscular movement, such as occurs with physical activity or exercise, massages lymph through the thoracic duct toward the subclavian vein. Several branches of lymph vessels feed into the thoracic duct as it courses through the chest, rejoining to form a single segment that intersects with the subclavian vein beneath the clavicle (collarbone).

For further discussion of the thoracic duct within the context of BLOOD and lymph structure and function please see the overview section "The Blood and Lymph."

See also LYMPH NODE; LYMPH VESSELS; RIGHT LYMPHATIC DUCT.

thrombocyte See PLATELET.

thrombocythemia A condition of the BLOOD in which the body overproduces platelets (also called thrombocytes), resulting in dysfunctional COAGULATION. Thrombocythemia, also called thrombocytosis, is a myeloproliferative disorder that can be primary (an independently occurring disorder, also called essential or idiopathic thrombocythemia) or secondary (a consequence of other health conditions or SPLENECTOMY). Doctors do not know what causes primary thrombocythemia, which occurs most commonly in people over age 50.

COMMON CAUSES OF SECONDARY THROMBOCYTHEMIA

INFECTION	INFLAMMATORY BOWEL DISEASE (IBD)
iron deficiency ANEMIA	LYMPHOMA
RHEUMATOID ARTHRITIS	SARCOIDOSIS
TUBERCULOSIS	Wegener's granulomatosis

Symptoms and Diagnostic Path

The excess platelets in the blood cause disturbances of coagulation that often result in these symptoms, which may be subtle or overt:

- easy bleeding, notably from the mucous membranes, such as frequent nosebleeds (EPISTAXIS), or from the gastrointestinal tract
- easy bruising
- clotting (thrombosis)
- SPLENOMEGALY (enlarged SPLEEN)
- HEADACHE or dizziness
- hemorrhage

A blood PLATELET level higher than 500,000 platelets per microliter (mc/L) of blood typically confirms the diagnosis, though the doctor may choose to do a BONE MARROW biopsy. Bone marrow biopsy shows an abundance of megakaryocytes, the parent cells of platelets, oversize platelets, and platelet fragments.

Treatment Options and Outlook

Treatment for secondary thrombocythemia targets the underlying condition, with resolution of the thrombocythemia after improvement in that condition. Treatment for primary thrombocythemia aims to suppress myeloproliferation (bone marrow cell production activity). Common forms of myelosuppressive therapy are radioactive phos-

phate and the CHEMOTHERAPY agents hydroxyurea and anagrelide. Some people benefit from platelet apheresis, a form of HEMAPHERESIS that removes platelets from the blood and returns all other blood components to the person. The doctor will closely monitor the complete blood count (CBC) as well as platelet function and coagulation during treatment, usually with weekly blood tests.

Primary thrombocythemia is a chronic condition that requires ongoing treatment. Many people will remain relatively symptom-free once treatment stabilizes platelet production. The condition takes a more serious course in some people who may experience worsening symptoms, notably hemorrhage. Rarely, primary thrombocythemia evolves into chronic myeloid LEUKEMIA (CML), a cancer of the bone marrow.

Risk Factors and Preventive Measures

Because doctors do not know what causes primary thrombocythemia, risk factors remain unknown and there are no known preventive measures. Early diagnosis and appropriate treatment offer the most optimal prognosis (outlook) to minimize the level to which the condition affects QUALITY OF LIFE.

See also POLYCYTHEMIA VERA; THROMBOCYTOPENIA.

thrombocytopenia A disorder of the BLOOD in which the blood contains too few platelets (also called thrombocytes), the cells active in COAGULATION (clotting). Thrombocytopenia, also called thrombopenia, is a secondary condition that develops as a consequence of prolonged bleeding, aplastic ANEMIA, blood disorders such as THROMBOCYTHEMIA, and cancers affecting the BONE MARROW.

POTENTIAL CAUSES OF THROMBOCYTOPENIA

acute idiopathic thrombopenia purpura	ANTIDIABETIC MEDICATIONS
AUTOIMMUNE THROMBOCYTOPENIA	aplastic ANEMIA
chronic ALCOHOL consumption	BLOOD TRANSFUSION reaction
CIRRHOSIS	chronic idiopathic thrombopenia purpura
GASTROINTESTINAL BLEEDING	heparin
HIV/AIDS	LEUKEMIA
MYELOFIBROSIS	PLATELET dysfunction
quinidine	rifampin
SEPTICEMIA	sulfa ANTIBIOTIC MEDICATIONS

Certain medications may also cause thrombocytopenia as an undesired SIDE EFFECT. Thrombocytopenia may occur when the bone marrow cannot produce enough platelets or when the SPLEEN and LIVER remove too many platelets from the blood.

Symptoms and Diagnostic Path

The characteristic sign of thrombocytopenia, regardless of its underlying cause, is excessive superficial bleeding. Symptoms include

- PETECHIAE, pinpoint hemorrhages beneath the surface of the SKIN that have the appearance of a RASH
- ECCHYMOSIS, a pattern of easy and excessive bruising with minor bumps and scrapes
- unprovoked bleeding from the nose (EPISTAXIS), gums, URETHRA, and other mucous tissues
- blood in the urine, stool, or vomit
- excessive bleeding with dental procedures or surgery
- signs of intracranial bleeding (bleeding within the skull)

A blood test that shows the low PLATELET count with normal counts and appearance of other blood cells is fairly conclusive of the diagnosis, especially when an underlying condition known to cause thrombocytopenia also is present. The doctor may choose to do a bone marrow biopsy. Because thrombocytopenia can be an early indication of HIV INFECTION, the doctor is also likely to do an HIV antibodies test to determine whether HIV infection is present.

Treatment Options and Outlook

Treatment depends on the underlying condition. Sometimes platelet transfusions are necessary to provide enough platelets for proper coagulation. Thrombocytopenia is not usually a life-threatening condition and typically resolves when the underlying condition improves.

Risk Factors and Preventive Measures

The primary risk factors for thrombocytopenia are the conditions that result in its development. Avoiding these factors, such as alcohol consumption or a medication that is causing thrombocytopenia as a side effect, or treating the condition

dispenses the likelihood for developing thrombocytopenia.

See also DISSEMINATED INTRAVASCULAR COAGULATION (DIC); THROMBOCYTHEMIA.

thymectomy A surgical OPERATION, performed under general ANESTHESIA, to remove the THYMUS, a structure of lymphatic tissue located behind the sternum (breastbone) that produces T-cells. Tendrils of the thymus often extend upward toward the THYROID GLAND and downward over the HEART. The loose structure of the thymus can make it challenging to surgically remove.

Thymectomy is the treatment of choice for most cancers of the thymus, which are uncommon. Doctors sometimes use thymectomy to treat severe AUTOIMMUNE DISORDERS, such as MYASTHENIA GRAVIS, as a method to restrict the body's ability to produce T-cells and thus limit the IMMUNE RESPONSE. Thymectomy in childhood has extensive consequences for IMMUNE SYSTEM development though does not appear to alter IMMUNE RESPONSE in adults. Most people require only a one or two day stay in the hospital, and about four to six weeks for full recovery.

See also LYMPHOCYTE; SPLENECTOMY.

thymus A structure of lymphatic tissue located in the upper central chest, behind the sternum (breastbone) midway between top of the HEART and the sternal notch at the base of the THROAT. The thymus is fairly large at birth, spreading in a loosely shaped "H" across the great vessels that emerge from the heart. The tissue of the thymus sometimes extends upward to make contact with the THYROID GLAND and downward to drape over the heart's upper chambers, the atria. Occasionally fragments of thymic tissue exist as unattached, isolated lobules typically remaining in the upper chest and lower neck.

The thymus is most active in youth, serving as the incubator in which T-cells, the lymphocytes crucial for the body's defense against INFECTION, mature and differentiate (acquire their functional characteristics). The thymus typically enlarges as a child approaches PUBERTY, its peak time of activity, then begins to recede. By midlife little more than strands of thymic tissue remain. The thymus also produces hormones—key among them being thymosin, thymulin, thymopoietin, and thymocyte humoral factor—that regulate T-cell maturation.

STATUS LYMPHATICUS: "ENLARGED" THYMUS

In the 1940s and 1950s, conventional medical wisdom blamed the large thymus of childhood for unexplained sudden death in children, conveying upon the condition the diagnostic label *status lymphaticus*. RADIATION THERAPY to shrink the thymus became the prevailing treatment. By the 1960s doctors recognized the thymus was normally large in children and abandoned the diagnosis and its treatment.

Researchers believe the thymus has other functions related to IMMUNE RESPONSE, though remain unable to determine their precise mechanisms. An infant born without a thymus has no ability to develop an IMMUNE SYSTEM; this CONGENITAL ANOMALY is nearly always fatal in infancy. There also appears to be a correlation between the thymus and MYASTHENIA GRAVIS, an autoimmune disorder in which the immune system produces antibodies that target acetylcholine, the NEUROTRANSMITTER that facilitates NERVE signals traveling between nerve cells and MUSCLE cells. An enlarged thymus is common in people who have myasthenia gravis and removing it (THYMECTOMY) often results in dramatic improvement in the condition. The thymus may have a role in other AUTOIMMUNE DISORDERS such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) and GRAVES'S DISEASE. Thymoma and thymic CARCINOMA are two forms of cancer that may develop in the thymus. Cancer of the thymus is uncommon.

For further discussion of the thymus within the context of blood and lymph structure and function please see the overview section "The Blood and Lymph."

See also HIV/AIDS.

V

vitamin K A vitamin that is a crucial catalyst, or coenzyme, in the COAGULATION process (also called coagulation cascade). Vitamin K (naphthoquinone) plays a role in activating seven of the CLOTTING FACTORS in various stages of coagulation, helping convert them from the inactive state in which they circulate in the BLOOD to active proteins that form clots. Vitamin K also is important for new BONE growth and BONE DENSITY. The major forms of vitamin K are phylloquinone (K1), menaquinone (K2), and menadione (K3, synthetic and cannot be converted into K1).

DIETARY SOURCES OF VITAMIN K

Food	Amount of Vitamin K per 1-Cup Serving
Kale, cooked	1,062 micrograms (mcg)
spinach, cooked	888 mcg
collard greens	836 mcg
parsley	324 mcg
Brussels sprouts, cooked	219 mcg
onions, spring	207 mcg
broccoli, cooked	220 mcg
lettuce, leaf (Bibb, Boston)	167 mcg
asparagus, cooked	144 mcg
prunes, stewed	65 mcg
lettuce, romaine	57 mcg
peas, cooked	40 mcg
blackberries, blueberries (fresh)	28 mcg
lettuce, head (iceberg)	13 mcg
turkey, cooked	5 mcg
strawberries, raw	4 mcg

Source: USDA National Nutrient Database for Standard Reference, SR17 Nutrients List: Vitamin K (Phylloquinone)

Most of the vitamin K the body uses is in the form of phylloquinone and comes from plant foods in the diet, notably leafy green vegetables such as spinach, kale, and broccoli. Intestinal BACTERIA also synthesize (manufacture) a small amount of vitamin K (menaquinone). Though vitamin K is fat soluble, the body does not maintain a significant store of it. Consequently, health experts have established daily adequate intake values of 90 micrograms per day for women and 120 micrograms per day for men.

The commonly used oral anticoagulant medication, warfarin, inhibits clotting by blocking the actions of vitamin K. Doctors may recommend restricting consumption of foods high in vitamin K for those who are taking ANTICOAGULATION THERAPY or maintaining consistent consumption of vitamin K–containing foods (not to exceed the daily adequate intake value) so the body's levels of vitamin K remain stable.

Because infants often have inadequate levels of vitamin K in their blood at birth, most hospitals in the United States administer vitamin K supplement injections to newborns within 24 hours of birth, which is the current recommendation of the American Academy of Pediatrics. Doctors do not agree on the value or effectiveness of routine vitamin K supplements in other circumstances. Most health experts recommend obtaining the body's supply of vitamin K through dietary sources, which is fairly easy for most Americans to do because a wide variety of foods contain this nutrient. Menadione is the synthetic supplement form of vitamin K.

See also ANTICOAGULATION THERAPY; OSTEOPOROSIS; VITAMINS AND HEALTH.

von Willebrand's disease A hereditary, genetic bleeding disorder resulting from a deficiency or

molecular abnormality of clotting factor VIII. Unlike HEMOPHILIA A, which also results from clotting factor VIII deficiency, von Willebrand's disease affects both men and women equally. Its inheritance pattern is autosomal dominant, meaning a child can acquire the condition when only one parent has the defective GENE. Von Willebrand's disease is the most common bleeding disorder in the United States, affecting about 1 percent of the American population. The condition is mild in most people, though severe trauma or major surgery may cause life-threatening hemorrhage especially in people who do not know they have the disorder.

Symptoms and Diagnostic Path

The most common symptom of von Willebrand's disease is somewhat prolonged bleeding with cuts, wounds, dental procedures, and surgeries. Easy bruising, frequent nosebleeds (EPISTAXIS), and bleeding gums are also common symptoms. Some people may periodically develop PETECHIAE, pinpoint hemorrhages beneath the surface of the SKIN that have the appearance of a RASH. Women who have von Willebrand's disease may have unusually heavy menstrual bleeding. The diagnostic path includes blood tests to measure clotting times, PLATELET AGGREGATION, and the level of von Willebrand factor multimers in the blood. The results of these diagnostic blood tests are usually conclusive for the diagnosis.

Treatment Options and Outlook

No treatment is necessary for people who have mild symptoms, though anyone diagnosed with von Willebrand's disease should carry or wear identification that alerts emergency medical personnel to the condition. Treatment before scheduled surgeries or for bleeding due to trauma is administration of PLASMA cryoprecipitate, which contains concentrated CLOTTING FACTORS, or purified factor VIII concentrate.

People who have von Willebrand's disease should not take NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), including aspirin, as these medications further decrease PLATELET AGGREGATION and increase bleeding.

Risk Factors and Preventive Measures

As von Willebrand's disease is hereditary, family history is the only known risk factor. People who have von Willebrand's disease may choose GENETIC COUNSELING before deciding to conceive children. Most people who have von Willebrand's disease experience little interference with QUALITY OF LIFE. The condition generally remains stable throughout life. Other health conditions that affect bleeding may result in a compound effect to produce more intense symptoms than either condition alone would otherwise manifest.

See also COAGULATION; GENETIC DISORDERS.

THE PULMONARY SYSTEM

The pulmonary system brings oxygen into the body and expels metabolic wastes in the form of gases. Physician specialists who treat conditions of the pulmonary system are internists who have subspecialty certifications in pulmonary medicine (pulmonologists). Physician specialists who operate on the LUNGS and related structures are thoracic surgeons. This section, "The Pulmonary System," presents an overview of the structures and functions of the pulmonary system, a discussion of pulmonary health and disorders, and entries about the health conditions that can affect the lungs and related structures.

Structures of the Pulmonary System

TRACHEA
BRONCHUS
bronchiole
ALVEOLUS
PLEURA
left lung
  upper lobe
  lingula (lingular segment)
  lower lobe
right lung
  upper lobe
  middle lobe
  lower lobe
DIAPHRAGM

Functions of the Pulmonary System

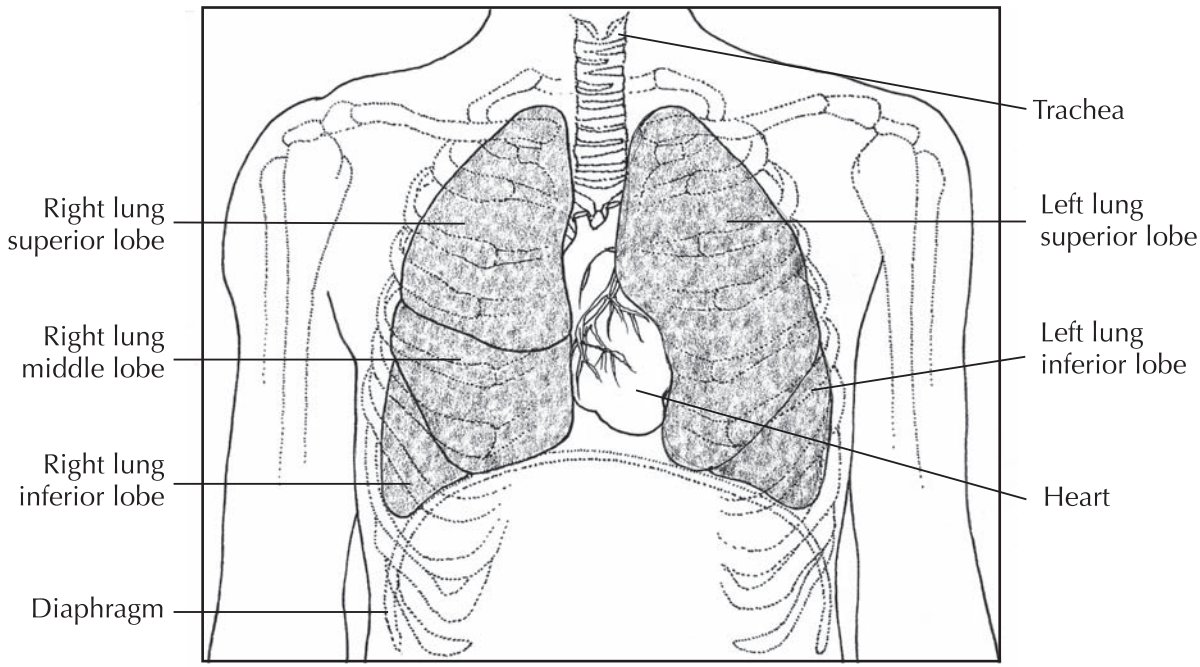
The LUNGS bring life-giving oxygen into the body and remove toxic gaseous wastes from it. An asymmetrical pair, these spongy structures rhythmically expand and compress about 15 to 20 times a minute. Expansion, or inhalation, draws air and oxygen into the lungs; compression, or exhalation, expels carbon dioxide and other gases that are metabolic waste byproducts of cellular activity. The structures of the nasal cavity and the upper airway (THROAT) bring air, containing about 21 percent oxygen, into the body. The NOSE and SINUSES warm and moisturize the air.

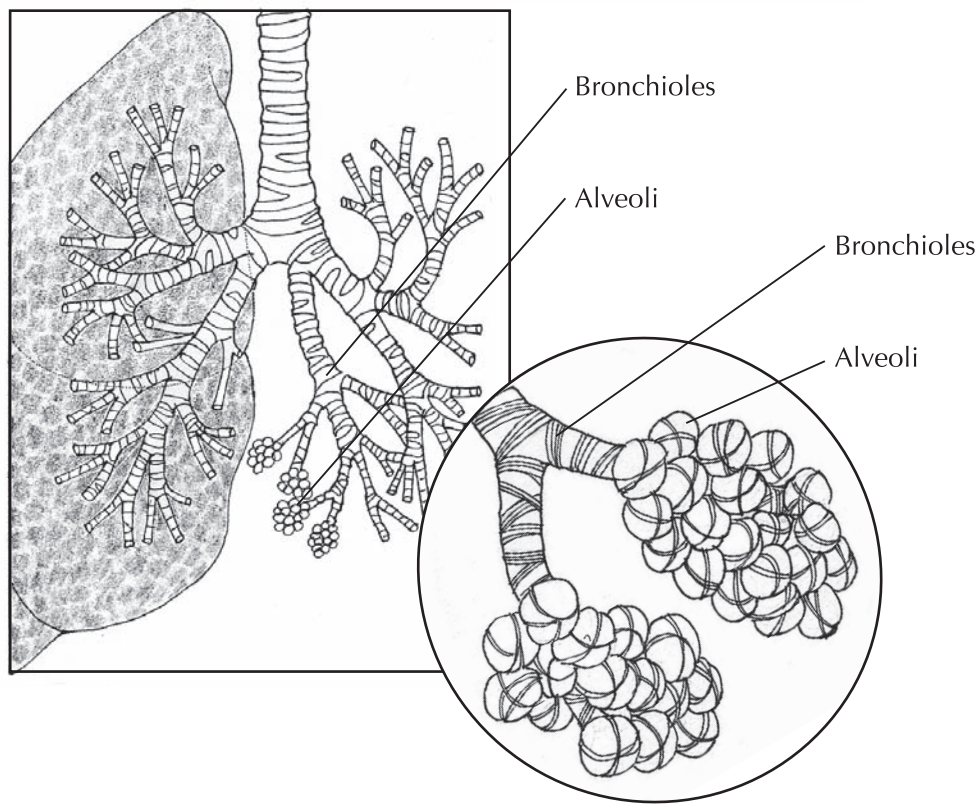
Carrying that air to the lungs are the TRACHEA, bronchi, and bronchioles—a branching structure of progressively smaller airways. The air's destination is the alveoli, tiny membranous sacs that cluster grapelike at the ends of the bronchioles. A webbing of capillaries (tiny blood vessels) surrounds each ALVEOLUS, carrying erythrocytes (red BLOOD cells) waiting to receive oxygen molecules and release carbon dioxide molecules. This process, the OXYGEN–CARBON DIOXIDE EXCHANGE, gives the body life.

LOBES AND SEGMENTS OF THE LUNGS

Right Lung	Left Lung
Right upper lobe	***Left upper lobe***
apical segment	apical-posterior segment
posterior segment	anterior segment
anterior segment	superior lingular segment (lingula)
Right middle lobe	inferior lingular segment (lingula)
lateral segment	***Left lower lobe***
medial segment	superior segment
Right lower lobe	anterior basal segment
superior segment	lateral basal segment
anterior basal segment	posterior basal segment
medial basal segment	
lateral basal segment	
posterior basal segment	

The lungs: asymmetry in synchronization The lungs fill the thoracic cavity from neck to DIAPHRAGM and sternum to spine. Though paired, the lungs differ somewhat in structure. The right lung is larger than the left lung, containing three lobes to the left lung's two. The left lung must accommodate the HEART, which nestles into an indentation called the cardiac notch. Some anatomists consider the small tail of tissue in the left lung that drops behind the heart, called the lingula, as a structure separate from either lobe of the left lung though most designate it a segment of the left upper lobe. Each lobe of the lung further contains structural divisions called bronchopulmonary segments, 10 among the three


Trachea
Right lung superior lobe
Left lung superior lobe
Right lung middle lobe
Left lung inferior lobe
Right lung inferior lobe
Heart
Diaphragm


Bronchioles
Alveoli
Bronchioles
Alveoli

lobes of the right lung and 8 among the two lobes of the left lung. A bronchial cluster—which includes bronchi, bronchioles, alveoli, blood vessels, LYMPH VESSELS, and nerves—branches into each segment.

The cells of the respiratory tract are primarily epithelial cells, the same kind of cells that make up the SKIN. The epithelial cells lining the trachea and bronchi contain cilia, tiny hairlike projections that sweep debris, such as dust and pollen, and excess mucus from the respiratory tract outward to the throat for coughs to expel them from the body. A tissue-thin membrane, the PLEURA, covers the outer surface of the lungs. The pleura secretes serous fluid to lubricate the lungs in their perpetual movement, protecting them from friction and irritation. Lung tissue is highly porous, with the substance of the lungs being about 15 percent solid tissue and 85 percent air and blood.

The heart pumps the body's full volume of blood—about five liters—through the lungs once each minute to pick up oxygen and release carbon dioxide. The blood, which flows through the lungs in a closed circuit from the heart via the PULMONARY ARTERIES and back to the heart via the PULMONARY VEINS, pulses through a dense, meshlike capillary network surrounding the alveoli. Pulmonary and cardiovascular mechanisms maintain an intricate balance between the flow of blood and the flow of air, with the blood flow constantly adjusting to flood into CAPILLARY BEDS surrounding alveoli that have strong air flow and recede from those with diminished air flow. This balance provides the greatest efficiency for getting oxygen into the bloodstream.

The bronchial tree: trachea, bronchi, bronchioles, and alveoli Like a hollow trunk, the trachea supports the treelike bronchial structure that brings air into the lungs. The trachea extends from the back of the throat about four and a half inches down to the midchest, where it branches into the right BRONCHUS and left bronchus. The spine in the back and the sternum in the front protect the trachea's path. The trachea's most vulnerable exposure is at the front of the neck, where it passes in front of the ESOPHAGUS before dropping behind the sternal notch. C-shaped bands of CARTILAGE help protect the trachea as well as give it the rigidity necessary to maintain an open passageway against ever-changing air pressures. Long fibers of smooth MUSCLE complete the posterior wall of the trachea.

The trachea terminates with the branching of the right main bronchus, going to the right lung, and left main bronchus, going to the left lung. Like the trachea, the bronchi contain smooth muscle with rings of cartilage for support and STRENGTH. The smooth muscle fibers of the trachea and the bronchi contract and expand in response to the air pressure changes of inhalation and exhalation. Each bronchus quickly divides to branch to the lung's lobes (lobular bronchi), and further subdivides into segmental bronchi, branching bronchi, and ultimately the very tiny and cartilage-free bronchioles. The alveoli cluster at the ends of the bronchioles.

The alveoli are the work stations of the lungs, and each lung contains about 150 million of them. Each microscopic alveolus looks like a small sac; an alveolar cluster contains dozens of alveoli that bubble from the end of a bronchiole. The alveolar membrane, the thickness of a single cell, forms the interface between the pulmonary system and the cardiovascular system, allowing the oxygen and carbon dioxide molecules to cross from the air within the lungs and the blood within the capillaries. Their bunched arrangement vastly extends the surface area available for oxygen exchange within the confined space of the chest. The total surface area of the alveoli, if spread out flat, is about the size of a tennis court.

Breathing: mechanics, physics, and molecular exchange The balance between oxygen and carbon dioxide in the blood regulates pulmonary respiration (BREATHING). As carbon dioxide from cellular METABOLISM accumulates in the blood, it reaches a threshold that triggers a sequence of biochemical signals to the brainstem. The brainstem then initiates a RESPIRATORY CYCLE, sending NERVE signals that trigger the diaphragm (the flat, broad muscle that forms the base of the thoracic cavity) and the intercostal muscles (the muscles between the ribs) to contract. In response the diaphragm flattens, pulling the floor of the thoracic cavity downward. The intercostal muscles simultaneously contract to pull the ribs outward and upward. The synchronized movements enlarge the thoracic cavity, drawing air into the lungs. When the diaphragm and the intercostal muscles

relax, the thoracic cavity returns to its resting size and the lungs expel air.

With each breath the EPIGLOTTIS, a flap of cartilaginous tissue at the back of the throat, opens and closes like a valve to allow air to pass in and out of the trachea and to keep other substances (such as saliva, food, and drink) from entering the trachea and lungs. With the changing of air pressure that occurs between inhalation and exhalation, oxygen molecules migrate through the micrometers-thin membrane walls of the alveoli into the blood circulating through the capillaries that surround the alveoli. Carbon dioxide molecules cross back in exchange. The respiratory cycle repeats about 20,000 times every 24 hours, varying in rate according to the body's oxygen needs.

ALTITUDE AND OXYGEN

Though the *percentage* of oxygen in the air remains constant regardless of altitude, the *concentration* of oxygen molecules decreases as altitude increases. The concentration of oxygen molecules in the air is greater at sea level than in the mountains. At a higher altitude the LUNGS must work harder to extract enough oxygen to meet the body's needs. In the short term the body compensates by raising the RESPIRATION RATE—breathing faster. After about 72 hours at a higher altitude, the decreased concentration of oxygen in the air stimulates the BONE MARROW to produce more erythrocytes (red BLOOD cells), which increases the blood's capacity to carry oxygen.

Health and Disorders of the Pulmonary System

The lungs rhythmically pull air into and release air from the body in a choreography the BRAIN coordinates with the HEART RATE and BLOOD PRESSURE to maintain the vital supply of oxygen to tissues throughout the body. Aerobic conditioning through regular physical exercise, not smoking, and maintaining healthy weight are among the key factors that keep the lungs functioning efficiently across the span of life.

Lung capacity peaks during the 20s and gradually declines with increasing age. People who remain aerobically fit continue to have strong pulmonary function despite this decline, as their lungs still have enough reserve to meet the body's needs. People whose lifestyles are sedentary are more likely to experience a decline in lung capacity, apparent in shortness of breath when climbing stairs, when walking distances, or with sudden bursts of physical exertion.

The lungs are subject to few BIRTH DEFECTS. Congenital disorders of the lungs include hereditary disorders, such as CYSTIC FIBROSIS, and conditions resulting from prematurity or inadequate development of the lungs before birth, such as chronic lung disease of infancy. Cardiovascular anomalies, notably structural malformations such as transposition of the great arteries (TPA) or hypoplastic left heart syndrome (HLHS), affect the integration of function between the heart and the lungs.

Cigarette smoking, CARDIOVASCULAR DISEASE (CVD), and long-term exposure to irritants such as industrial chemicals are the leading causes of acquired pulmonary disease. Because the lungs face continual exposure to external pathogens, they are vulnerable to viral, bacterial, and fungal invaders. Immune cells—notably lymphocytes, macro-phages, and neutrophils—reside within the walls of the bronchi, detecting and eliminating most pathogens before they can cause localized INFECTION. However, those that slip through the body's defense mechanisms can cause serious diseases such as PNEUMONIA (viral or bacterial).

HEALTH CONDITIONS THAT CAN AFFECT THE STRUCTURES OF THE PULMONARY SYSTEM

ANTHRACOSIS	APNEA
ASBESTOSIS	ASPERGILLOSIS
ASPIRATION	ASTHMA
ATELECTASIS	BERYLLIOSIS
BRONCHIECTASIS	BRONCHITIS
BYSSINOSIS	CHRONIC OBSTRUCTIVE
CYSTIC FIBROSIS	PULMONARY DISEASE (COPD)
LEGIONNAIRES' DISEASE	INTERSTITIAL LUNG DISORDERS
LUNG CANCER	LUNG ABSCESS
Pneumocystis carinii	PLEURISY
PNEUMONITIS	PNEUMONIA
PULMONARY EDEMA	pulmonary congestion
PULMONARY FIBROSIS	PULMONARY EMBOLISM
RESPIRATORY FAILURE	PULMONARY HYPERTENSION
tuberculosis	SILICOSIS

Inefficient cardiovascular function places significant strain on pulmonary function, influencing

the respiratory rate as well as pressuring the network of blood vessels within the lungs to cause conditions such as PULMONARY HYPERTENSION. Congestive HEART FAILURE develops when the heart is not strong enough to pump blood throughout the body, allowing fluids to seep from the bloodstream and into the interstitial spaces in the lungs. The resulting pulmonary congestion and PULMONARY EDEMA fills the lungs with fluid, restricting the oxygen–carbon dioxide exchange. Exposure to environmental irritants and toxins also can damage the lungs, particularly as a cumulative effect over time, causing repeated INFLAMMATION that can result in SCAR formation (fibrosis).

Traditions in Medical History

Ancient Western and Eastern medical traditions alike correlated the function of the lungs with the role of bringing life-giving air, and the NUTRIENTS it bears, into the body. Greek physician Galen (129–199), whose views framed the perceptions and practices of medicine for nearly 1500 years, postulated the lungs took in and digested air, after which the pulmonary VEIN carried the resulting "vapors" to the heart. Though this hypothesis held the correct intent, its details were enough skewed to thwart genuine understanding of cardiopulmonary circulation for centuries.

The concepts of cardiovascular circulation and pulmonary function finally began to converge with William Harvey's detailed monograph, *Exercitatio Anatomica De Motu Cordis et Sanguinis in Animalibus*, published in 1628. This work, whose title translates as *A Treatise on the Movement of the Heart and Blood in Animals*, provided the first definitive description of the circulation of the blood through the heart, lungs, and blood vessels. Harvey failed to identify the capillary beds and their role in oxygen–carbon dioxide exchange; yet his work established the foundation for later researchers to make this and other discoveries about lung function.

Once physicians understood the basic functioning of the lungs, heart, and blood, they could begin to find the causes of the diseases that disrupted these functions, often with debilitating or fatal results. Throughout documented history, TUBERCULOSIS—consumption, as early cultures called this infection that appeared to "consume" its sufferers—has reigned as one of the most devastating diseases known to afflict humankind. The disease causes inflammation, granulation, and calcification within the inner structures of the lungs, permanently destroying lung tissue. Unchecked, tuberculosis spreads within the infected person to fully involve the lungs and often other organs such as the KIDNEYS, spinal fluid, and bones. Early explanations for tuberculosis, which accounted for about 1 in every 20 deaths across centuries and civilizations, ranged from dietary habits such as eating meat and drinking liquor to environmental exposures such as foul weather and smoke from burning fires. In fact, however, tuberculosis spreads among people through contact with bacteria in the SPUTUM (the mucus, fluids, and debris coughed from the lungs) of those who are infected.

Ancient Egyptian mummies demonstrate BONE damage characteristic of tuberculosis. Even famed Western physician of antiquity and Galen's predecessor Hippocrates (460–400 B.C.E.) wrote of the physical wasting that accompanied tuberculosis and warned against close contact, even by physicians, with those in the end stages of the disease. Not for nearly two millennia after him, however, did physicians make the connection between close contact and the contagiousness of tuberculosis. In 1882 microbiologist Robert Koch (1843–1910) discovered the responsible bacillus, *Mycobacterium tuberculosis*, turning the corner toward finding a true cure for the infectious and debilitating disease. Though a cure was still another 60 years away, isolating those who were ill became the trend. Doctors sent those afflicted with tuberculosis to sanatoriums where fresh air, rest, and nutritious meals formed the core of treatment. It was enough for some, though not most, people to recover or at least to send the disease into inactivity—and it separated the infectious from the healthy, helping slow contagion. Some people underwent more dramatic therapies, such as intentional collapse of the infected lung, to try slow the progression of the disease by starving the tissue of oxygen.

In 1943 biochemist Selman Waksman was able to isolate and cultivate an effective antibiotic, streptomycin, to kill *M. tuberculosis* without also killing the person this stubborn PATHOGEN infected. By the early 1960s researchers had developed a regimen of multiple antibiotics to successfully cure

tuberculosis, and over the next 20 years tuberculosis dramatically subsided in developed countries. Tuberculosis resurfaced as a significant health threat with the emergence of HIV/AIDS in the 1990s, however, with new strains of the bacillus that were resistant to previously successful antibiotics. New generations of antibiotics have become available, though *M. tuberculosis* continues to mutate into resistant forms. Today, this destructive infection of the lungs persists.

With the advent of modern industrialization came a surge of induced diseases, many of which exposed the lungs to various particulates such as coal dust (miner's lung), silica (grinder's rot), and plant fibers (mill FEVER). These and other occupational lung diseases have disabled and killed millions of people through the centuries and continue to threaten health even today despite precautions to reduce the risks of exposure.

Miner's lung (ANTHRACOSIS), also called black lung, once disabled nearly every coal miner who worked longer than a few years in the mines and today remains a significant occupational disease threat. SILICOSIS, long a risk for workers in occupations with exposure to sand dust, appears in the lungs of mummies from ancient Egypt, a consequence of the intensely blowing sands of the region, and in the lungs of contemporary workers in quarries, potteries, and industries that use sandblasting. Although new exposures to asbestos are uncommon, the long time from exposure to the development of disease means symptoms arise in people today whose exposure through employment (such as shipbuilding or insulation work) took place decades ago. Though not as common as before modern ventilation and dust control mechanisms became commonplace, long-term inhalation of cotton fibers by textile workers results in BYSSINOSIS—mill fever.

Today lung disease related to industrial practices remains a key component of public health. The use of respirators, exhaust venting, and exposure limitations helps reduce, but does not completely prevent, occupational lung diseases. Some of these conditions are treatable; others are progressive or cause permanent damage. General air pollution resulting from industrial and motor vehicle exhaust accounts for much ASTHMA, chronic BRONCHITIS, PNEUMONITIS, and other ailments of the lungs. ENVIRONMENTAL CIGARETTE SMOKE (secondhand smoke) has further emerged as a dangerous and potentially lethal toxin of exposure. The air that bears life-giving oxygen also transports, sometimes unknowingly, the agents of lung damage.

OCCUPATIONAL LUNG CONDITIONS

ANTHRACOSIS	ASBESTOSIS
ASTHMA	BERYLLIOSIS
BYSSINOSISchronic BRONCHITIS	HYPERSENSITIVITY PNEUMONITIS
INTERSTITIAL LUNG DISORDERS	mesothelioma
PULMONARY FIBROSIS	SILICOSIS

Breakthrough Research and Treatment Advances

The unraveling of the human GENOME has produced significant breakthroughs in understanding and treating health conditions affecting all body systems. Key discoveries related to pulmonary disorders have in particular improved treatment for CYSTIC FIBROSIS, once a disease that claimed the lives of its victims before they reached ADOLESCENCE. Today it is more common than not for those who have cystic fibrosis to enjoy reasonable QUALITY OF LIFE into their early 30s, with new treatments based on GENE THERAPY showing great promise for arresting the progress of this debilitating genetic disorder. LUNG TRANSPLANTATION is emerging as a promising, viable treatment for end-stage pulmonary disease resulting from disorders such as cystic fibrosis, pulmonary hypertension, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), and PULMONARY FIBROSIS.

A

acute respiratory distress syndrome (ARDS) A complex of symptoms, formerly called adult respiratory distress syndrome, in which respiratory distress and RESPIRATORY FAILURE develop accompanying severe illness or trauma. ARDS involves the whole of both LUNGS, as the lungs become inflamed and fill with fluid. ARDS may develop as a consequence of injury that directly affects the lungs (notably blunt trauma to the chest, near drowning, PNEUMONIA, and smoke inhalation) or when the injury or illness affects other parts or systems of the body. Systemic INFECTION (SEPSIS), DRUG OVERDOSE, and BLOOD TRANSFUSION may also result in ARDS. ARDS can affect people of any age and is life-threatening. Because people who develop ARDS are already very ill, ARDS has a high death rate (about 40 percent). The syndrome may cause complete respiratory failure or lead to total system failure, either of which presents significant challenge for recovery.

Symptoms and Diagnostic Path

People who develop ARDS have generally sustained severe trauma or infection and most are already in the hospital when their symptoms begin. Early symptoms of ARDS include restlessness, TACHYPNEA (rapid, shallow breathing), and HYPOXIA (reduced oxygen to the body's tissues). ARDS progresses rapidly to full involvement of the lungs. Chest X-rays show the filling of the lungs with INFLAMMATION and fluid (called diffuse infiltration). Arterial BLOOD gases show the decreased percentage of oxygen in the blood. Doctors often perform tests on SPUTUM and fluid from the lungs to identify any pathogens, notably BACTERIA, that may be present.

Treatment Options and Outlook

Immediate oxygen supplementation is essential. Many people require MECHANICAL VENTILATION with positive end expiratory pressure (PEEP) to increase the amount of oxygen entering the lungs. Doctors generally administer sedation while the person is on mechanical ventilation, to provide comfort and to prevent the natural tendency to fight the intervention. Treatment primarily is supportive, including close monitoring of cardiovascular and renal (kidney) functions. Because infection, either in the lungs or elsewhere in the body, is often present, many people may also receive intravenous (IV) ANTIBIOTIC MEDICATIONS.

The outlook for full recovery depends on numerous factors including the person's age, general health status, and the ability to reverse the circumstances responsible for the initial development of ARDS. Even medical intervention that begins early in the course of ARDS cannot predict the success of treatment. About 60 percent of people survive the ARDS episode, though the severity of illness can require extensive recuperation.

Risk Factors and Preventive Measures

The primary risk factors for ARDS are sepsis (severe infection) and major trauma, either to the lungs or to the body in general. Though such infection or trauma alerts doctors to the grave risk for ARDS, there are no known measures that can head off the development of ARDS. Public health measures to minimize the risk factors (trauma and infection) are critical. Once ARDS occurs, however, aggressive medical intervention and support provide the best chance for survival.

See also HEART FAILURE; SEVERE ACUTE RESPIRATORY SYNDROME (SARS).

aging, pulmonary changes that occur with The LUNGS and tracheobronchial structures undergo few but significant changes over the course of the life-

span. From moments after birth to near the end of life the lungs function continuously and consistently, bringing air into the body to deliver oxygen to the BLOOD and carrying air out of the body to eliminate carbon dioxide and other gaseous metabolic wastes from the body. The entire respiratory process—BREATHING and oxygenation—takes place under the regulation of the brainstem, without conscious awareness or control.

Before birth, though the lungs go through the movements of breathing they do not oxygenate the fetus's blood. Rather, the fetus draws its oxygen from the mother's blood through the PLACENTA where oxygen molecules migrate across the capillary membranes from the mother's blood supply to the fetus's blood supply. Differences in the cardiovascular system of the fetus further support this mechanism of oxygenation. In the unborn child the HEART shunts blood from the right atrium to the left atrium through an opening in the atrial septum (wall of muscle that separates the right atrium and the left atrium) called the foramen ovale. Blood also passes from the PULMONARY ARTERIES to the AORTA through an opening called the ductus arteriosus, bypassing the lungs.

The newborn's first breath fills the lungs with air, setting in motion a sequence of events that results in the closure of these openings in the heart and the rerouting of blood flow from the right side of the heart to the lungs and from the lungs to the left side of the heart. As the lungs fully expand after a few breaths, they take over complete responsibility for oxygenating the body. The lung tissue produces a chemical called surfactant, a fluid that coats the inner layer of the lung surfaces to maintain appropriate surface tension to keep the alveoli from collapsing with each exhaled breath, much in the same fashion moisture inside a balloon keeps the walls of the balloon from sticking together when the balloon deflates. These changes may lag in an infant born prematurely, giving rise to breathing and oxygenation difficulties until the lungs can more fully develop.

The lungs continue to function in the same responsibility for the remainder of life, with few changes beyond growing as the body grows. Lung capacity (the ability of the lungs to hold air) and diffusing capacity (the ability of the lungs to transfer oxygen to the blood) peak in the early 20s, after which both slowly but steadily decline until by about age 75 they are roughly half what they were at age 25. Beginning at age 35, lung capacity diminishes about 5 percent every 10 years. In the 50s the muscles of breathing begin to stiffen and lose resilience, though in counterbalance changes within the lungs and airways occur to reduce the resistance air encounters during inhalation. Regular aerobic CONDITIONING throughout life can offset many of the functional implications of these changes, allowing strong pulmonary performance well into the 70s or beyond.

The health conditions affecting the lungs before age 30 tend to be acute (of sudden onset and contained duration), often INFECTION such as viral or bacterial BRONCHITIS, pleuritis, and PNEUMONIA. Chronic (ongoing) health conditions affecting the lungs become increasingly common with advancing age, in part because the natural changes in the lungs may precipitate them and in part because other health situations or environmental factors begin to have cumulative consequences.

CARDIOVASCULAR DISEASE (CVD), which becomes more common in middle age and beyond among both men and women, can have as much effect on the structures and functioning of the pulmonary system as do conditions of the lungs. HEART FAILURE, in which the heart cannot pump enough blood to meet the body's oxygen needs, allows fluid to back up into the lungs. The resulting circumstances, pulmonary congestion and PULMONARY EDEMA, flood the alveoli and prevent them from conducting the OXYGEN–CARBON DIOXIDE EXCHANGE. Chronic HYPERTENSION (high BLOOD PRESSURE) diminishes the elasticity of all arteries in the body, including the pulmonary arteries. The resulting stiffness and inflexibility of the arteries can contribute to or exacerbate cardiovascular conditions such as heart failure. Other forms of cardiovascular disease may result in PULMONARY HYPERTENSION, increased pressure within the pulmonary arteries that damages the smaller arteries within the lungs.

External factors also influence pulmonary health throughout life. Cigarette smoking is the single-most destructive exposure the lungs typically face, causing an extremely high risk for progressive disorders such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) and especially for LUNG CANCER. Cigarette smoking accounts for 85 percent

of lung cancer in the United States. Over time breathing exposes the respiratory tract to numerous insults from substances such as environmental pollution, viruses, BACTERIA, pollens, dust, and other materials. These exposures may injure or damage the lungs, resulting in conditions such as ASTHMA, PNEUMONITIS, bronchitis, and pneumonia, as well as infections such as TUBERCULOSIS and INFLUENZA. Such pulmonary conditions can contribute to deteriorating lung functions, particularly in people who have not maintained adequate AEROBIC FITNESS.

Maintaining a steady level of AEROBIC FITNESS through regular physical activity keeps the pulmonary system as healthy as possible for as long as possible, helping offset the changes of advancing age. Aerobic fitness enables the lungs to efficiently extract oxygen from the air and conduct it into the bloodstream. As well, the lungs fill more fully with air on each inhalation, keeping the alveoli open and functioning. This helps keep fluid from accumulating within the alveoli.

See also AGING, CARDIOVASCULAR CHANGES THAT OCCUR WITH; AGING, CHANGES IN THE BLOOD AND LYMPH THAT OCCUR WITH; ASPIRATION; CONGENITAL HEART DISEASE; PLEURISY; SMOKING AND HEALTH.

alveolus A tiny, thin-walled sac, grouped in clusters at the ends of the smallest airways (bronchioles) deep inside the LUNGS, that is the terminus for each breath of air. A dense mesh of capillaries entwines each alveolus. Oxygen from the air within the alveolus passes across the alveolar membrane to enter the bloodstream, while carbon dioxide and other waste gases pass across the membrane from the BLOOD to the air within alveolus. The clustered formations of the alveoli greatly increase the surface area for OXYGEN–CARBON DIOXIDE EXCHANGE. Each lung contains about 300 million alveoli, which, if spread out, would coat the surface of a tennis court—about 290 square feet. The large surface area is important but so is the very thin interface between the airway and the blood vessel. Many disease states cause this barrier to thicken or distort, which impedes the exchange of oxygen and carbon dioxide (called decreased diffusing capacity).

For further discussion of the alveolus within the context of pulmonary structure and function please see the overview section "The Pulmonary System."

See also BRONCHUS; HEMOGLOBIN; TRACHEA.

anthracosis A lung condition resulting from long-term exposure to coal dust, also called coal worker's PNEUMONOCONIOSIS (CWP) and black lung disease. There are two types of anthracosis: simple and complicated. In simple anthracosis the coal dust coats the LUNGS in wide distribution, and the IMMUNE RESPONSE encapsulates the dust particles without causing scarring (fibrosis). This is the most common type of anthracosis and may generate no symptoms or mild symptoms such as DYSPNEA (shortness of breath) with exertion and chronic COUGH. The doctor may detect simple anthracosis during routine medical examination or screening for lung disease. Diagnosis generally considers X-RAY findings in combination with history of exposure to coal dust. The doctor may also conduct BRONCHOSCOPY to examine the inner bronchial structures, which have a characteristic black appearance.

Complicated anthracosis becomes aggressively fibrotic, though doctors do not know what causes it to do so. It continues to progress even after exposure ends, and may result in disabling obstructive lung disease. Symptoms include worsening cough and dyspnea. About 15 percent of coal workers who have simple anthracosis develop complicated anthracosis.

Improvements in mining techniques and conditions, including environmental filtration systems, have greatly reduced the amount of dust coal mining operations produce. Those who work as cutters, loaders, and continuous mining operators face the highest risk for exposure. In the United States, the Occupational Safety and Health Administration (OSHA) regulates permissible levels of dust and worker exposure. Diagnosis of new cases of anthracosis is steadily declining as a result. Federal health programs provide medical care and other benefits for coal workers who have anthracosis.

See also ASBESTOSIS; BERYLLIOSIS; BYSSINOSIS; CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD); SILICOSIS.

apnea The temporary and involuntary cessation of BREATHING. Apnea may result from neurologic

causes (central apnea), mechanical causes (obstructive apnea), or a combination of both. Central apnea is more common in premature infants, whose nervous systems are not fully developed, and the very elderly, whose nervous systems may be failing. Central apnea is also more common in people who have underlying neurologic disorders or who have heart failure. Obstructive apnea may occur in children who have greatly enlarged tonsils or adenoids and in individuals who have OBESITY. Some people have irregular breathing patterns that are, for them, normal. A doctor should evaluate irregularities in breathing to determine whether the circumstances merit medical intervention.

Most people who have apnea are unaware of apneic episodes, though others who observe them may become alarmed (especially parents or caregivers who notice apnea in young children). Recurrent apnea that occurs during sleep, called OBSTRUCTIVE SLEEP APNEA, is a serious health condition that disrupts the sleeping patterns and results in sleep deprivation though most people are not aware of this because they do not have conscious recollection of the apneic episodes. Researchers believe that severe and persistent obstructive sleep apnea contributes to cardiovascular conditions such as HEART FAILURE.

The diagnostic path includes careful analysis of apnea patterns, taking into consideration the person's age, the onset of the apnea, and adverse effects that may result (including effects resulting from sleep deprivation). The pulmonologist may conduct pulmonary function tests, BLOOD tests to measure levels of erythrocytes (red blood cells) and HEMOGLOBIN in the blood, and X-rays or other diagnostic imaging procedures to look for obstructive causes. A comprehensive NEUROLOGIC EXAMINATION, including ELECTROENCEPHALOGRAM (EEG), may reveal the cause of central apnea.

Treatment targets the underlying cause of the apnea. For some people, surgery to remedy the cause of an obstruction may provide long-term relief (such as TONSILLECTOMY and ADENOIDECTOMY in children who have enlarged tonsils and adenoids). Central apnea that results from damage to the brainstem or other underlying neurologic disorder can be difficult to treat. Oxygen therapy alone may help with some central apneas.

See also ASPHYXIA; CHEYNE-STOKES RESPIRATION; DYSPNEA; SUDDEN INFANT DEATH SYNDROME (SIDS); TACHYPNEA.

asbestosis Damage to the LUNGS resulting from inhalation of asbestos fibers. During the first half of the 20th century asbestos, a natural substance mined from underground, became common in insulating materials because of its natural heat resistance. In the 1950s researchers linked chronic asbestos inhalation with PULMONARY FIBROSIS and a rare form of LUNG CANCER, mesothelioma, found almost exclusively in people with asbestos exposure. In the 1970s the United States implemented strict regulations that prohibited the use of asbestos in many of its formerly common applications. For people who had occupational exposure to asbestos before these restrictions, however, asbestosis is a significant risk. Millions of Americans live with asbestosis and hundreds die each year from it or from lung cancer associated with asbestos exposure.

Asbestos fibers embed in the tissues of the lungs, causing INFLAMMATION and granulation that eventually leads to fibrosis (SCAR tissue formation). Some forms of asbestos are more hazardous than others. Typically lung damage from asbestos takes 20 years or longer after exposure to manifest. The likelihood of developing health consequences from asbestos exposure correlates directly to the amount of asbestos and the duration of the exposure. Cigarette smokers face increased risk, particularly of lung cancer, as the asbestos and the carcinogenic chemicals in cigarette smoke potentiate each other (intensify each other's actions in the lungs).

Symptoms and Diagnostic Path

Many people do not show symptoms of asbestosis until the damage is fairly advanced. Because of this, health experts recommend people with known asbestos exposure receive annual examinations to monitor the health of their lungs. When symptoms manifest they typically include

- DYSPNEA (difficulty BREATHING) with physical exertion
- dry (nonproductive) COUGH
- chest discomfort, tightness, or PAIN

The diagnostic path includes comprehensive work and health histories, physical examination including AUSCULTATION, chest X-rays, and sometimes other diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI). Finger clubbing, in which the ends of the fingers become thick, rales (crackling BREATH SOUNDS), and CYANOSIS (bluish hue to the lips and SKIN that signals inadequate oxygenation) are common signs of lung damage typical of lung diseases such as asbestosis. Doctors assign a numeric classification from grade 0 to grade 4 to indicate the severity of damage, along with letter designations A, B, or C to identify the extent of lung structure affected.

Treatment Options and Outlook

Treatment for asbestosis is largely supportive, as it is not possible to remove the fibers once they embed in the lungs. SMOKING CESSATION is of prime importance, as cigarette smoking in combination with asbestos exposure greatly increases the likelihood of lung cancer. Treatment also targets specific concerns or other problems as they arise. Generalized efforts to promote pulmonary health, such as BREATHING EXERCISES and regular physical activity to improve AEROBIC CAPACITY, increase the efficiency of undamaged lung tissue.

Because the latency period (time between exposure and symptoms) is so long, damage to the lungs can be quite extensive by the time symptoms become apparent. People who know they have had exposure to asbestos should have regular pulmonary examinations to monitor for asbestosis. Though asbestosis can be fatal, many people live without significant complications due to the condition. The most significant consequence of asbestosis is lung cancer, including mesothelioma, a type of lung cancer that only occurs with asbestos exposure.

Risk Factors and Preventive Measures

Asbestosis only occurs as a consequence of asbestos exposure, so eliminating exposure eliminates the risk of developing the condition. Preventive measures for those who continue to have occupational exposure include appropriate protective clothing and respirators.

See also ANTHRACOSIS; BERYLLIOSIS; BYSSINOSIS; LIVING WITH CHRONIC PULMONARY CONDITIONS; SILICOSIS; SMOKING AND PULMONARY DISEASE.

aspergillosis An opportunistic fungal (yeast) INFECTION that can manifest as PNEUMONIA in people who have HIV/AIDS, are undergoing CHEMOTHERAPY to treat cancer, receive IMMUNOSUPPRESSIVE THERAPY

ASBESTOSIS SEVERITY

Grade	Severity	Extent of Lung Damage
grade 0	asymptomatic	asbestos fibers present but no fibrosis
grade 1	mild damage	fibrosis limited to bronchi and bronchioles, no alveolar involvement
grade 2	moderate damage	fibrosis extends to alveoli
grade 3	serious damage	fibrosis extends between alveolar clusters
grade 4	severe damage	fibrosis obliterates alveoli, replacing them with honeycombed SCAR tissue
grade a	mild involvement	scattered bronchial structures are involved
grade B	moderate involvement	fewer than half the bronchial structures are involved
grade C	severe involvement	greater than half the bronchial structures are involved

after ORGAN TRANSPLANTATION, or are otherwise IMMUNOCOMPROMISED. Aspergillosis may also occur as an allergic reaction (called allergic bronchopulmonary aspergillosis or ABPA) in people who have ASTHMA or CYSTIC FIBROSIS, causing airway INFLAMMATION and fluid accumulation in the LUNGS. *Aspergillus*, the infective FUNGUS, is common in the environment, especially in decaying vegetation and in the soil, and in air ventilation ducts in buildings. Hospitals also harbor *Aspergillus*, so aspergillosis can develop as a nosocomial infection. Occasionally aspergillosis takes the form of an encapsulated ball, called an aspergilloma or a mycetoma, that forms within a pocket of healed SCAR tissue from previous damage to the lung such as may remain from TUBERCULOSIS or SARCOIDOSIS.

Symptoms and Diagnostic Path

Symptoms of aspergillosis vary widely and may not appear at all unless the fungus establishes itself within the lungs in a widespread pattern. When symptoms are present they typically include

- HEMOPTYSIS (bleeding from the lungs that appears in the SPUTUM or coughing up BLOOD)
- CHEST PAIN
- FEVER
- COUGH
- rapid or difficult BREATHING (DYSPNEA)

The doctor also may suspect aspergillosis in a person who has been receiving treatment for an apparent bacterial infection without any improvement in symptoms. The diagnostic path typically begins with a chest X-RAY, which shows whether there are infiltrates or obstructions in the lungs. COMPUTED TOMOGRAPHY (CT) SCAN often can provide more detailed visualization of lung structures and anomalies. Though imaging results are not conclusive, they provide leading clues to suggest or rule out aspergillosis. Because aspergillosis spores are so common in the environment, sputum cultures are not usually helpful in making the diagnosis as nearly everyone's sputum is likely to contain some *Aspergillus*. BRONCHOALVEOLAR LAVAGE, in which the pulmonologist rinses cell samples from the walls of the bronchi during BRONCHOSCOPY, or biopsy to obtain tissue samples, may provide more accurate culture results. The individual's health history also plays a key role in making the diagnosis.

Treatment Options and Outlook

Invasive aspergillosis is life-threatening and requires treatment with intravenous (IV) ANTIFUNGAL MEDICATIONS such as amphotericin B, itraconazole, or voriconazole. Recovery depends on the IMMUNE SYSTEM's ability to rally against the infection. In people who are immunocompromised, the challenge may be overwhelming. In such situations aspergillosis can have serious and even fatal consequences. However, most people fully recover with appropriate treatment. Aspergillomas may require surgery to remove them when they cause bleeding (evident as hemoptysis), pain, or difficulty breathing. CORTICOSTEROID MEDICATIONS such as prednisone are usually effective in relieving the symptoms of ABPA, which is an immune reaction to the presence of *Aspergillus,* common in people who have asthma, rather than an invasive infection with the fungus.

Risk Factors and Preventive Measures

People who are taking immunosuppressive therapy, such as after organ transplantation, or who are immunocompromised are vulnerable to invasive aspergillosis because their immune systems cannot fend off this ordinarily innocuous fungus. Aspergillosis is also a risk for people who have HIV/AIDS. Though there are no measures for preventing aspergillosis, those who are susceptible to this fungal infection can minimize the severity of disease by seeking medical diagnosis and treatment at the earliest indication of disease.

See also BRONCHIECTASIS; NEUTROPENIA.

asphyxia The inability of the LUNGS to take in air or conduct the OXYGEN–CARBON DIOXIDE EXCHANGE, depriving the body of oxygen.

Asphyxia is a life-threatening emergency that requires immediate medical treatment.

Asphyxia may occur as a consequence of water or other fluids in the lungs (drowning) that results in suffocation (inability of air to enter the lungs), carbon monoxide poisoning, trauma to the TRA-

CHEA (windpipe), injury to the brainstem affecting the NERVOUS SYSTEM signals that regulate breathing, compression of the neck or chest, electrical shock, cardiovascular collapse, and other circumstances that interfere with BREATHING. A person experiencing asphyxia may require immediate CARDIOPULMONARY RESUSCITATION (CPR) until medical care is available.

See also HYPOXIA.

aspiration Drawing foreign matter, often food or drink, into the airways (TRACHEA and bronchi). The COUGH REFLEX typically activates to expel the matter, though may not succeed if inhalation draws the matter deep into the respiratory tract or the cough reflex is weak. Food, drink, and other substances that coughing does not expel can lodge in the airway to create a partial or complete obstruction.

Aspiration is potentially life-threatening and may require emergency intervention such as the HEIMLICH MANEUVER. A doctor should evaluate the condition of the LUNGS when aspiration occurs.

Material that makes its way deep into the LUNGS is likely to draw BACTERIA and fluid to the site, establishing inflammation, edema, PNEUMONIA, or LUNG ABSCESS. Physical movement such as sitting, standing, and walking may help the respiratory tract propel the substance outward, while inactivity allows the matter to settle into the lungs. Near drowning often results in aspiration of water into the lungs.

A chest X-RAY typically shows the site of INFLAMMATION and fluid collection. Treatment may require BRONCHOSCOPY to retrieve the object and ANTIBIOTIC MEDICATIONS to treat INFECTION. Aspiration pneumonia is a potentially serious condition, particularly in the elderly, infants, and debilitated people who cannot easily move around or who may have trouble with the natural mechanisms that protect the airway, resulting in foreign matter getting into the lungs. Aspiration pneumonia develops when the accumulated fluid becomes infected or interferes with the ability of the lungs to oxygenate the BLOOD.

See also BRONCHUS.

asthma A disease of the airways that results in narrowing of the airways (bronchospasm) and INFLAMMATION in response to a wide range of inhaled irritants such as pollen, mold, smoke, chemicals, and the airborne debris of pests ranging from cockroaches to microscopic dust mites. This narrowing, or airflow obstruction, is usually reversible when the person can eliminate the exposure or through treatment with medications called bronchodilators. Repeated exposure to irritants in susceptible people can result in repeated episodes of inflammation. This pattern can ultimately cause scarring of the airways that is not reversible.

Nearly 18 million Americans have asthma, a third of whom are under age 18. For many of them asthma attacks are mild and infrequent, giving the perception that asthma is a common and, though annoying, harmless condition. However, life-threatening consequences can occur during a severe asthma attack. If the person does not receive rapid and effective treatment, the airway narrowing and inflammation can completely block the flow of air. The person cannot exhale (breathe out) fully, lowering oxygen levels and potentially causing death. Nearly 5,000 Americans die each year as a consequence of asthma or its complications.

Symptoms and Diagnostic Path

An asthma attack generally follows a pattern of symptoms that, though it varies among people who have asthma, tends to be consistent for each individual. Some people first experience DYSPNEA (shortness of breath) or wheezing (a high-pitched whistling sound with exhalation), for example, while other people find a restless night with frequent waking foreshadows an asthma attack that manifests the following day. Common symptoms of asthma attacks include

- dry, nonproductive COUGH
- sense of tightness in the chest
- dyspnea, especially during physical activity
- wheezing
- gasping for air

There are no definitive tests for asthma. The diagnostic path may include tests and procedures,

such as chest X-RAY and complete BLOOD count (CBC), to rule out other causes of symptoms. The pulmonologist will conduct pulmonary function tests to measure the flow and volume of air, typically before and after administration of a bronchodilator medication that relaxes and opens the airways. People who have asthma generally have much improved pulmonary function test results after the bronchodilator, even when they are having no symptoms of asthma at the time of testing. However, the reverse can also be true and the person has normal breathing tests during a time of no symptoms. In such cases, the pulmonologist may conduct a test called a methacholine challenge, administering the DRUG methacholine to see whether it initiates a mild hypersensitivity reaction. A positive response (symptoms appear) is fairly conclusive of an asthma diagnosis.

Treatment Options and Outlook

Treatment for many people who have asthma is a combination of medications to prevent symptoms (long-acting, controller medications) and to provide immediate relief from symptoms that occur (short-acting, rescue medications). Medication regimens vary with the step (classification) and nature of symptoms. Commonly prescribed medications include

- inhaled (and occasionally oral) CORTICOSTEROID MEDICATIONS, which are anti-inflammatory and serve as long-term controller medications
- inhaled and oral beta-2 agonists, which are bronchodilators and may provide short-acting or long-acting relief
- leukotriene modifiers, which are IMMUNE RESPONSE mediators that provide long-term control

The mainstay of asthma treatment is baseline control of the inflammation with long-acting medications. For some people, ALLERGY DESENSITIZATION (when allergy reaction is the clear cause of the asthma) provides further control. Other important steps for managing asthma long-term include monitoring asthma symptoms (such as with peak flow monitoring) and developing an action plan for asthma control. When there is an acute exacerbation of symptoms (an asthma attack), treatment is most likely to succeed when it begins in advance of or immediately on recognition of symptoms. Once an asthma attack is under way, even rescue medications may take time to bring the situation under control.

Lifestyle factors for managing asthma include avoiding known triggers and allergens. Three of the most common triggers are allergic RHINITIS, chronic SINUSITIS, and GASTROESOPHAGEAL REFLUX DISORDER (GERD). Regular physical exercise, though for some people a trigger for asthma attacks, generally improves lung capacity, pulmonary efficiency, and AEROBIC FITNESS. Air-conditioning helps reduce humidity in the air and filter the air of particulates that may cause irritation or exacerbate asthma symptoms. It is important to regularly change the air filters for central heating and cooling systems. ACUPUNCTURE treatments are helpful for reducing the frequency and severity of asthma attacks in some people.

ASTHMA CLASSIFICATION

Classification	Severity	Frequency of Symptoms Without Treatment
step 1	mild intermittent	symptoms occur two days or less each week and two nights or less each month
step 2	mild persistent	symptoms occur up to five days each week and up to five nights in a month
step 3	moderate persistent	symptoms occur at least once during every day and several nights a week
step 4	severe persistent	symptoms occur throughout the day, every day, and most nights

MEDICATIONS TO TREAT ASTHMA

Type of Medication	Common Products	Type of Relief	Asthma Classification
beta-2 agonists, inhaled	albuterol (Airet, Proventil, Ventolin), bitolterol (Tornalate), pirbuterol (Maxair)	short-acting rescue	steps 1, 2, 3, or 4
beta-2 agonists, oral	long-acting: salmeterol (Serevent), albuterol extended release (Volmax, Proventil Repetabs) short-acting: terbutaline (Brethine, Bricanyl)	long-acting: controller medication, especially at night short-acting: rescue	steps 2, 3, and 4
corticosteroids, inhaled	beclomethasone (Qvar, Vanceril), budesonide (Pulmicort), flunisolide (AeroBid), fluticasone (Flovent), triamcinolone (Azmacort)	long-acting controller medication	steps 2, 3, and 4
corticosteroids, oral	methylprednisolone (Medrol), prednisone (Deltasone, Orasone), prednisolone (Prelone)	short-acting controller medication for symptoms that do not respond to other medications rescue	steps 3 and 4
leukotriene modifiers, oral	zafirlukast (Accolate), zileuton (Zyflo)	long-acting controller medication	steps 3 and 4, occasionally step 2
other, inhaled	ipratropium (Atrovent), cromolyn (Intal), nedocromil (Tilade)	short-acting rescue prophylactic when used before intense physical exercise	steps 3 and 4
other, oral	theophylline (Theo-Dur, Theolair, Aerolate, Slo-Phyllin)	long-acting	step 3, occasionally step 2

Risk Factors and Preventive Measures

The key risk factor for asthma attack is exposure to a substance that initiates a hypersensitivity reaction. Most people can easily identify these substances after experiencing a few asthma attacks, and avoiding exposure to known allergens significantly reduces attacks. A wide range of irritants can cause asthma attacks in many people, however, making it impossible to avoid exposure. As well, for some people triggers for asthma attacks include emotional stress and physical exertion, common elements of everyday life.

Health experts have identified a number of factors that appear to increase an individual's risk for developing asthma. Key among them are

- living in cities, where the concentration of particulate pollutants in the air is high
- family history of asthma
- recurrent upper respiratory INFECTION as a child
- cigarette smoking or exposure to ENVIRONMENTAL CIGARETTE SMOKE

- long-term or repeated exposure to chemicals such as cleaning solutions, paints, industrial chemicals used in manufacturing, pesticides and herbicides, and aerosols
- presence of ALLERGIC RHINITIS, atopic DERMATITIS, or chronic SINUSITIS

Viral infections, physical exertion such as with exercise, cold air, sulfite preservatives (common in some foods), some medications, and GASTROESOPHAGEAL REFLUX DISORDER (GERD) also may trigger asthma attacks. Researchers do not know why some people develop hypersensitivity reactions to certain substances while other people, even though their immune systems similarly create antibodies, experience normal reactions. Though researchers believe there are likely genetic factors that underlie allergies, they have yet to isolate them.

See also ALLERGIC ASTHMA; ANTIBODY; ATOPY; BREATH SOUNDS; HYPERSENSITIVITY REACTION; LIVING WITH CHRONIC PULMONARY CONDITIONS; MULTIPLE CHEMICAL SENSITIVITY SYNDROME.

atelectasis The collapse of a segment or lobe of the lung, or an entire lung. Atelectasis is fairly common and most often spontaneously corrects itself for full recovery. The collapse may result from obstruction, structural damage to lung tissue, fibrosis that destroys bronchial segments, PNEUMOTHORAX, PLEURAL EFFUSION, and other causes. A form of chronic atelectasis, right middle lobe syndrome, results from chronic INFLAMMATION of the LYMPH nodes near the area, which are beneath the right lung's middle lobe. A common cause of atelectasis is taking shallow breaths, which is common in people coming out of ANESTHESIA but still sedated after surgery or who have abdominal or chest wall pain.

Symptoms and Diagnostic Path

Symptoms of atelectasis vary with the rate of onset and the extent of lung area involved. Rapid collapse may cause sharp PAIN and sudden DYSPNEA and may also cause severe COUGH. Chronic atelectasis or atelectasis that develops gradually may produce few symptoms, though many people develop a persistent, nonproductive cough.

The diagnostic path begins with careful AUSCULTATION for BREATH SOUNDS. Typically the collapsed segment causes displacement within the thoracic cavity of the affected lung, and often the unaffected lung as well as the HEART. Breath sounds may be normal though heard in abnormal locations. The doctor may also hear wheezes or rales, abnormal breath sounds that suggest blocked airways. Chest X-RAY clearly shows the displacement and the extent of the collapse. In the simplest case, coughing and deep breathing may resolve the atelectasis. In other cases, the doctor may desire additional diagnostic imaging such as COMPUTED TOMOGRAPHY (CT) SCAN to precisely identify the site of the atelectasis as well as the possible cause (such as a tumor or an obstruction). BRONCHOSCOPY may allow the pulmonologist to directly visualize the collapsed area and remove an obstruction such as a foreign object or mucus plug, if that is the cause of the collapse. Bronchoscopy also permits BRONCHOALVEOLAR LAVAGE or biopsy, if indicated.

Treatment Options and Outlook

Often, segmental atelectasis requires no treatment beyond watchful waiting or encouraging deep breathing. The lung will correct itself. Infection requires treatment with ANTIBIOTIC MEDICATIONS; inflammation may require treatment with CORTICOSTEROID MEDICATIONS. Other medications that sometimes relieve discomfort and help the lung restore itself include bronchodilators, which relax and open the airways. CHEST PERCUSSION AND POSTURAL DRAINAGE help keep the lungs free from accumulated secretions, and the doctor may recommend the person lie on his or her unaffected side to allow gravity to help restore the collapsed segment. Rarely, the doctor may consider surgery for chronic atelectasis that fails to respond to medical treatment. Most people recover from atelectasis without complications.

Risk Factors and Preventive Measures

Risk factors for atelectasis include obstructive pulmonary conditions such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), CYSTIC FIBROSIS, chronic BRONCHITIS, and BRONCHIECTASIS. Recent surgery with general anesthesia is a common cause of atelectasis. Though avoiding these circumstances

may not be possible, being alert to the possibility of atelectasis allows medical evaluation and intervention before complications such as infection or PNEUMONIA establish themselves.

See also CYSTIC FIBROSIS AND THE LUNGS; LUNG CANCER; SMOKING AND PULMONARY DISEASE; SURGERY BENEFIT AND RISK ASSESSMENT.

auscultation The diagnostic procedure of listening to the LUNGS using a STETHOSCOPE held to various placements on the chest and back. Auscultation allows the doctor to hear normal and abnormal BREATH SOUNDS, the noises of air flowing through the respiratory tract. The doctor typically listens to the same location for each lung, to compare the sounds, and moves in a side-to-side pattern first across the chest from the apex to base (top to bottom) of each lung and then a similar pattern on the back. When conducting a pulmonary examination, the doctor also listens with the stethoscope placed over the TRACHEA at the throat.

There are four normal breath sounds—tracheal, vesicular, bronchial, and bronchovesicular—all heard upon both inhalation and exhalation. Deviations in tone, loudness, frequency, and character of the sounds help the doctor assess the performance of the lungs. Extra sounds, such as rales and wheezes, are abnormal and signal pulmonary ailments such as BRONCHITIS, ASTHMA, and PNEUMONIA. The doctor usually listens to the HEART as well during auscultation, as the HEART SOUNDS provide additional diagnostic information. The doctor uses the diaphragm of the stethoscope to auscultate for breath sounds and the bell of the stethoscope to auscultate for heart sounds.

See also APNEA; BREATHING; DYSPNEA; TACHYPNEA.

B

berylliosis Chronic damage to the LUNGS, also called chronic beryllium disease, resulting from industrial exposure to beryllium, a heavy metal that has many commercial uses and applications in contemporary manufacturing processes. Inhaled beryllium fumes and dust cause irritation to the delicate alveoli that activates the body's IMMUNE RESPONSE. In the United States berylliosis occurs primarily in people who work in the electronics, nuclear, and aerospace industries where beryllium usage is high. People who work in metal machining or alloy reclamation jobs are also at risk. The US Environmental Protection Agency (EPA) classifies beryllium dust and fumes as toxic substances, and the US Occupational Safety and Health Administration (OSHA) has established regulatory guidelines to minimize on-the-job beryllium exposure. Beryllium particles can remain in the lung tissues for six months to several years after exposure.

Berylliosis results from delayed-type hypersensitivity (DTH) in which helper T-cell lymphocytes flood the sites of exposure and encase the beryllium dust particles or the areas of INFLAMMATION, causing granulomas to form. Over time the granulomas evolve into fibromas, well-defined structures of SCAR tissue that replace normal lung tissue. As the penetration of granulomas and fibromas extends deeper into the lungs, the loss of alveolar function cripples the ability of the lungs to pass oxygen to the BLOOD.

Rarely, an individual may develop an immediate response, called acute chemical PNEUMONITIS, to beryllium exposure. Acute chemical pneumonitis requires prompt medical treatment to reduce airway irritation and INFLAMMATION.

Symptoms and Diagnostic Path

Symptoms of berylliosis are similar to symptoms of other chronic inflammatory diseases affecting the lungs, though employment in an occupation involving beryllium use is a key indication of the cause and nature of disease. Symptoms typically include

- chronic, nonproductive (dry) COUGH
- chest tightness or PAIN
- unintended weight loss
- shortness of breath (DYSPNEA), particularly with exertion
- fatigue

The diagnostic path includes chest X-RAY, BRONCHOALVEOLAR LAVAGE, and a specialized test called the beryllium lymphocyte proliferation test (BeLPT). The pulmonologist may also choose to perform high-resolution COMPUTED TOMOGRAPHY (CT) SCAN, which reveals small lesions within the lungs, and bronchial biopsy via BRONCHOSCOPY to further evaluate lesions that imaging procedures show. Pulmonary function tests and sometimes cardiopulmonary exercise testing can help assess the status of lung capacity and the ability of the lungs to oxygenate the blood. Conclusive diagnosis may require varied and numerous tests as well as thorough medical and personal histories, as berylliosis is similar to other interstitial lung diseases including sarcoidosis.

Treatment Options and Outlook

The first line of treatment is removal from the source of beryllium, which for most people means leaving the jobs that require exposure to beryllium. CORTICOSTEROID MEDICATIONS may help suppress the immune response and subdue the

inflammation. However, there is no known medical therapy to treat damage that has occurred to the lungs. Damage that does occur to the lungs is permanent and berylliosis is usually progressive, tending to continue even after exposure to beryllium ends. The resulting damage to the lungs may lead to HEART FAILURE and other cardiovascular health conditions because the HEART cannot pump enough BLOOD to oxygenate the body's tissues. LUNG TRANSPLANTATION may become a viable treatment option for people who develop complete pulmonary failure.

Risk Factors and Preventive Measures

Recent research suggests GENETIC PREDISPOSITION underlies most cases of berylliosis, with mutations or defects affecting the MAJOR HISTOCOMPATABILITY COMPLEX (MHC), which encodes aspects of immune response. The role of genetic predisposition is not entirely clear, though likely explains why some people who have limited exposure develop serious disease whereas others who have prolonged exposure seem to experience no adverse effects. However, berylliosis occurs only in people exposed to beryllium and nearly all such exposure is occupational, though beryllium is a natural mineral present in the environment. Reducing this exposure through appropriate occupational hygiene and protective measures can significantly reduce the risk of disease development.

MANUFACTURING JOBS WITH HIGH RISK FOR BERYLLIOSIS

aerospace alloys	computer electronics
dental alloys (bridges and crowns)	electrode welding
electronic resistors	heat sinks
jet brake pads	jet turbine blades
laser tubes	metal alloy bicycle frames
metal working	nuclear weapons
semiconductor chips	transistors
X-RAY windows	

People who work in industries in which beryllium use is common should be alert to the early symptoms of berylliosis. Contact with or use of products containing beryllium after their production or manufacture does not convey beryllium exposure, however. Screening blood BeLPT tests among people who work with beryllium can identify early indications of immune reactivity, allowing medical intervention to avert extensive damage to the lungs. OSHA recommends the use of powered respirators with high-efficiency particulate air (HEPA) filters and protective clothing in the workplace, as well as safeguards, such as showering and changing into complete street clothes (including shoes) before leaving the workplace.

See also ASBESTOSIS; BYSSINOSIS; ENVIRONMENTAL HAZARD EXPOSURE; HEAVY-METAL POISONING; OCCUPATIONAL HEALTH AND SAFETY; SARCOIDOSIS.

black lung See ANTHRACOSIS.

breathing The process of drawing air into and expelling air from the LUNGS, also called pulmonary respiration. Specialized centers in the brainstem regulate the rate and rhythm of respiration to harmonize breathing with HEART RATE and BLOOD PRESSURE. Breathing occurs through the mechanical actions of MUSCLE movement. The DIAPHRAGM (the large, flat muscle that extends across the floor of the thoracic cavity) and the intercostal muscles (the muscles between the ribs) contract to expand the thoracic cavity, pulling air into the lungs (inhalation). Inhalation is an active process.

Simultaneously the EPIGLOTTIS, a cartilaginous flap at the top of the throat normally closed across the top of the TRACHEA to prevent food and other materials from entering the lungs, opens to allow the air to pass. The air flows through the trachea into the bronchi, bronchioles, and alveoli. When the diaphragm and the intercostal muscles relax the thoracic cavity returns to its resting position, pressuring air out of the lungs (exhalation) in reverse sequence. Exhalation is a passive process.

Breathing patterns help the doctor assess pulmonary function and respiratory effectiveness. Breathing may be varying combinations of rapid (TACHYPNEA) or slow (bradypnea), regular or irregular, deep or shallow. Though an individual may influence breathing through conscious focus, breathing is an involuntary process under control of the brainstem. The concentration of carbon dioxide in the BLOOD is the primary trigger for initiation of a RESPIRATORY CYCLE (one inhalation and one exhalation), triggering the brainstem to signal the diaphragm and the intercostal muscles to contract.

See also BREATH SOUNDS; HYPERVENTILATION; RESPIRATION RATE.

breathing exercises Methods to improve lung capacity. Breathing exercises are especially helpful for people who have chronic or progressive lung conditions such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), BRONCHIECTASIS, and PULMONARY FIBROSIS. The pulmonologist or respiratory therapist may prescribe specific breathing exercises to accommodate an individual's unique needs and health status. General breathing exercises often recommended include

- belly breathing, which uses the abdominal muscles to help completely fill and empty the LUNGS
- pursed lip breathing, which releases air through lips formed as though to whistle and maintains positive pressure in the airways with exhalation (especially helpful for people who have COPD and other obstructive diseases)
- measured breathing, in which the person breathes in, holds the breath, and breathes out for an equal count at each stage

YOGA breathing is also beneficial for pulmonary health, with yoga breathing exercises to practice in combination with yoga positions as well as simply as breathing exercises. In yoga, the breath is *prana*, the energy of life, and breathing exercises are *pranayama*. Common *pranayama* include

- bellows breathing, in which inhalation is steady and full, with exhalation forceful and rapid
- alternate nostril breathing, in which inhalation is steady and full through one nostril with the fingers holding the other nostril closed, and exhalation through the other nostril, again with the fingers holding the nonbreathing nostril closed
- holding the breath, in which inhalation is steady and full, the lungs hold the breath for as long as is comfortable, and exhalation is steady and slow

For people who have pulmonary health conditions, breathing exercises are more challenging than they sound. It is important to begin slowly and progress steadily. The doctor should approve any planned exercise effort, including breathing exercises. Breathing exercises, including yoga's *pranayama*, are also highly effective for relaxation and stress reduction.

See also AEROBIC EXERCISE; AEROBIC FITNESS; DISABILITY AND EXERCISE; OXYGEN SATURATION; WALKING FOR FITNESS.

breath sounds Characteristic noises the flow of air makes as it courses through the TRACHEA and bronchi. The doctor listens to breath sounds using the diaphragm (flat) side of a STETHOSCOPE placed at various sites on the outside of the chest and the back, a diagnostic method called AUSCULTATION. There are four normal breath sounds, heard with inhalation and exhalation:

- Tracheal breath sounds, hollow sounds heard over the THROAT as air passes through the trachea
- Bronchial breath sounds, harsh sounds heard near the sternum as air passes through the bronchi (large airways in the LUNGS)
- Vesicular breath sounds, rustling sounds heard in most locations on the chest and back as air moves in and out of the alveoli
- Bronchovesicular breath sounds, a mix of harsh and rustling sounds heard just to the sides of the upper sternum on the chest and below the shoulder blades on the back

Normal breath sounds are of nearly equal duration with inhalation and exhalation and are particular to specific locations. Normal breath sounds heard elsewhere are abnormal and indicate the possibility of pulmonary conditions such as ATELECTASIS (collapsed segment of lung), fibrosis (SCAR tissue in the lungs), or other circumstances that cause the lung to shift its physical or functional presence within the thoracic cavity. The absence of normal breath sounds indicates that the segment or lobe of the lung is not receiving air, usually as a result of a significant bronchial occlusion (blockage of a bronchus), severe atelectasis, or lung collapse.

Other breath sounds the doctor can hear through the stethoscope are abnormal and indicate INFECTION or disease. Doctors call these adventitious breath sounds. Among them are

- wheezes, steady high-pitched whistling noise heard with exhalation that is typical of obstructed airways such as might result with ASTHMA, inhaled foreign objects, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), and chronic BRONCHITIS
- rales (also called crackles), intermittent crackling noises that may sound fine (like crinkling cellophane) or coarse (like pulling apart a hook and loop fastener) often heard with ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS), PULMONARY EDEMA, BRONCHIECTASIS, and INTERSTITIAL LUNG DISORDERS
- rhonchi, low-pitched, continuous whistling noises heard with exhalation that suggest airways blocked with mucus
- stridor, loud wheezing sounds heard with inspiration when there is an obstruction of the trachea

Stridor is a life-threatening emergency that requires immediate medical attention.

- pleural rub, brushing sounds that indicate INFLAMMATION of the PLEURA (membrane covering the outer surfaces of the lungs) such as occurs with PLEURAL EFFUSION or pleural fibrosis

Breath sounds present important diagnostic information that helps the doctor determine the health status of the lungs as well as assess the progress of conditions under treatment.

See also EPIGLOTTITIS; HEART SOUNDS.

bronchiectasis The dilation of a segment of BRONCHUS. Bronchiectasis may involve several bronchial branches and usually occurs deep within the lung, often in a lower lobe. Though bronchiectasis may be congenital (present at birth) or acquired (develop after birth), congenital bronchiectasis is rare and results when only the core structure of the LUNGS develops and existing bronchi dilate in reaction to the pressure of incoming air. Acquired bronchiectasis commonly develops with chronic lung INFLAMMATION such as results from CYSTIC FIBROSIS or repeated INFECTION (typically chronic BRONCHITIS).

Bronchiectasis represents permanent damage to lung tissue, often with accompanying PULMONARY FIBROSIS (scarring), and loss of lung function in the affected areas. Because of the lung's segmented structure nonaffected segments and lobes of the lung continue to function normally, so the extent to which the bronchiectasis affects respiratory performance depends on the number of segments involved. However, bronchiectasis tends to be progressive.

Suspicion of bronchiectasis becomes valid with the existence of pulmonary conditions known to be predisposing, such as cystic fibrosis and chronic bronchitis. Bronchiectasis may follow recurrent PNEUMONIA, ASPIRATION pneumonia, childhood diseases such as PERTUSSIS (whooping COUGH) in children who have not received IMMUNIZATION, and toxic inhalation (such as smoke or chemical inhalation). IMMUNODEFICIENCY disorders that increase the risk for pulmonary infections also raise the likelihood of bronchiectasis. Symptoms typically develop over months to years and commonly include

- persistent, productive cough more intense in the mornings and just before going to bed
- prodigious SPUTUM production
- HEMOPTYSIS (BLOOD in the sputum)
- wheezing (high-pitched, abnormal BREATH SOUNDS with exhalation)

The diagnostic path includes chest X-rays and COMPUTED TOMOGRAPHY (CT) SCAN. The doctor may further desire BRONCHOALVEOLAR LAVAGE or bronchial biopsy (via BRONCHOSCOPY), sputum cultures, and blood tests. Treatment depends on the findings and may include ANTIBIOTIC MEDICATIONS to treat infections or CORTICOSTEROID MEDICATIONS to treat severe inflammation. Bronchodilator medications may help relax and open undamaged bronchi to improve lung capacity. CHEST PERCUSSION AND POSTURAL DRAINAGE help loosen mucus so the normal mechanisms of the respiratory tract can move it out of the lungs. Rarely, surgery to remove a particularly eroded or chronically infected bronchial segment is necessary. Most people are able to manage bronchiectasis with regular medical evaluation and care (including prompt treatment at the earliest indication of infection).

Regular physical activity and avoiding cigarette smoke are crucial to preserve remaining lung function.

See also ATELECTASIS; AUSCULTATION.

bronchitis INFLAMMATION of the bronchi, the airways that branch from the TRACHEA into the LUNGS. Bronchitis may be viral, bacterial, or the result of irritation such as cigarette smoking or exposure to environmental pollutants. It may also occur as an acute condition that comes on suddenly, runs its course, and heals without lasting damage or persistently recur as a chronic condition.

Acute bronchitis Acute infectious bronchitis is especially common during the "cold and flu" season, when it typically follows a viral INFECTION of the upper respiratory tract. Numerous viruses may be responsible, including ADENOVIRUS, coronaviruses, INFLUENZA viruses, and rhinoviruses. Acute viral bronchitis generally runs its course over a period of five to seven days, during which the person feels and appears ill. A residual COUGH may persist for several weeks after the infection subsides.

Acute irritative bronchitis develops in response to inhaled irritants such as fumes, dust, and smoke (cigarette as well as environmental). Symptoms may be difficult to distinguish from those of ASTHMA, particularly in people who do not have a diagnosis of asthma or who have infrequent asthma attacks. The inhaled substance irritates the lining of the bronchi, causing localized inflammation. Most often, the inflammation and resulting bronchitis subsides over the course of a few days.

Chronic bronchitis Repeated exposure to irritants such as cigarette smoke, occupational chemicals, and environmental pollutants may cause persistent or recurrent bronchial inflammation. By far the most common culprit is cigarette smoking or environmental cigarette smoke exposure (second-hand smoking). The hallmark symptom is persistent, productive cough that continues for three months or longer. Over time, chronic bronchitis may evolve into CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) or BRONCHIECTASIS, two conditions in which damage to the bronchi is extensive and permanent. People who have chronic bronchitis are more vulnerable to bacterial infections such as PNEUMONIA, as well as to complications such as ATELECTASIS (collapse of a bronchial segment).

Symptoms and Diagnostic Path

The symptoms of acute bronchitis include FEVER, productive cough, sore THROAT, and chest discomfort or PAIN, especially when taking a deep breath. SPUTUM that is thick, yellowish green, and foul-smelling suggests bacterial infection. Red or brown streaks in the sputum indicate bleeding, which may be from the irritation of coughing or signal a different diagnosis. The diagnostic path includes AUSCULTATION to listen to BREATH SOUNDS, which are typically normal. The doctor may request a chest X-RAY to rule out other causes of the symptoms. The doctor may also collect a sputum sample for culture if there is any suspicion the infection could be bacterial.

The primary symptoms of chronic bronchitis are productive cough and DYSPNEA (shortness of breath). Physical exertion tends to exacerbate both. The diagnostic path begins with auscultation, which may reveal abnormalities of breath sounds depending on whether there is damage to the bronchial structures. Chest x-ray may show areas of inflammation as well as atelectasis or bronchiectasis if either is present. The doctor is likely to conduct further diagnostic procedures to rule out other conditions that could cause similar symptoms, such as asthma or, especially in smokers, LUNG CANCER.

Treatment Options and Outlook

Treatment for acute viral bronchitis is primarily supportive and targets symptom relief. The doctor may recommend a cough suppressant or an OVER-THE-COUNTER (OTC) DRUG such as acetaminophen to relieve fever and discomfort. It is important to drink lots of fluids to maintain HYDRATION and to thin bronchial secretions. When fever persists or recurs after acute infectious bronchitis, the likelihood of bacterial infection is high in which case treatment with ANTIBIOTIC MEDICATIONS becomes necessary. Antibiotics are not helpful for viral bronchitis, however. The doctor may prescribe an inhaled corticosteroid medication to suppress the inflammatory response in acute irritative bronchitis. Bronchodilators may also help if the bronchitis causes bronchospasm and wheezing.

The most effective treatment for chronic bronchitis is removing the cause of the symptoms, which most often is cigarette smoking. Chronic bronchitis becomes inevitable at some point in everyone who smokes. People who work in environments with high exposures to fumes, dust, or pollutants should use appropriate protective gear including masks or respirators. Chronic bronchitis that continues unchecked results in permanent damage to the bronchial structures.

Risk Factors and Preventive Measures

Frequent HAND WASHING is the best defense against viral infections of any sort. Upper respiratory viruses spread through droplet contamination, which may occur through direct touch (such as shaking hands) or breathing droplets coughed or sneezed into the air by those who have upper respiratory viruses. In epidemic circumstances, doctors may prescribe antiviral medications such as rimantadine to reduce the risk or severity of infection. Removal from the source of irritation reduces symptoms to improve chronic bronchitis. People who have high risk of respiratory infection, such as those who have chronic lung disease or other chronic health conditions, should receive influenza vaccination (flu shot) every year and pneumonia vaccination every five years.

See also ANTIBIOTIC RESISTANCE; CROUP; HEMOPTYSIS; PNEUMONITIS; SMOKING AND PULMONARY DISEASE.

bronchoalveolar lavage A diagnostic procedure that washes cells from the bronchi and alveoli for laboratory examination. The doctor does bronchoalveolar lavage during BRONCHOSCOPY, blocking a small section of the bronchial segment to instill and then withdraw sterile saline. The solution contains cells from the inner lung structures that can provide diagnostic information. The doctor may also use bronchoalveolar lavage therapeutically, to irrigate (rinse away) thickened mucus or other deposits from the LUNGS in conditions when thick plugs of mucus block the airways and do not respond to other treatments.

See also ALVEOLUS; BRONCHUS.

bronchoscopy A diagnostic procedure in which the doctor uses a flexible, lighted endoscope, inserted through the THROAT and into the airways under sedation or ANESTHESIA, to view the TRACHEA, bronchi, and other structures of the respiratory tract. The doctor also can watch the LUNGS in motion, assessing air movement and filling. Bronchoscopy is an outpatient procedure that takes about an hour. Many people receive mild sedation before the bronchoscopy to help them relax and be more comfortable.

The bronchoscope is a thin, flexible, lighted tube with a tiny camera on the tip. The pulmonologist sprays a topical anesthetic on the back of the throat to block the GAG REFLEX and numb the throat, then inserts the bronchoscope through the MOUTH (or the NOSE, with lubrication) and throat into the trachea. The pulmonologist guides the bronchoscope into the bronchi, which enables examination of the lung to a moderate depth of about four or five branchings of the bronchus. The pulmonologist may use bronchoscopy to obtain tiny tissue samples for biopsy or to perform BRONCHOALVEOLAR LAVAGE to obtain bronchial and alveolar cell samples. Bronchoscopy may also be therapeutic, allowing the pulmonologist to rinse accumulated mucus and debris from the bronchi.

It is common to feel some discomfort after the topical anesthetic wears off, similar to a sore throat. The discomfort generally does not last more than a day or two. Rarely after a biopsy, bronchoscopy may cause a PNEUMOTHORAX, a condition in which air gets in the pleural space (a small area around the lung) and the lung collapses. The risks of bronchoscopy for most people are minimal.

See also ALVEOLUS; BRONCHUS; ENDOSCOPY.

bronchus A secondary branch of the airways that connect the LUNGS and the primary airway, the TRACHEA. The main bronchi branch directly from the trachea at about mid-lung, with the right main bronchus channeling air to the right lung and the left main bronchus directing air to the left lung. Each main bronchus nearly immediately branches into lobular bronchi, three in the right lobe and two in the left lobe. Bronchi become diminishingly smaller as they branch deeper into the lungs. Rings of CARTILAGE give larger bronchi rigidity and support. Smaller bronchi have fewer and thinner cartilage rings, and bronchioles, the tiniest of the bronchi, have thin walls of only

smooth MUSCLE tissue with no cartilage. The bronchi are susceptible to irritation, INFLAMMATION, and INFECTION. When inflamed or irritated the bronchi can cause difficulty breathing (DYSPNEA).

For further discussion of the bronchi within the context of pulmonary structure and function please see the overview section "The Pulmonary System."

See also ALVEOLUS; ASTHMA; BRONCHIECTASIS; BRONCHITIS.

byssinosis A lung disorder resulting from extended exposure to the dust from cotton, flax, or other textile fibers. Also called brown lung, cotton worker's lung, or cotton bract disease, byssinosis is an occupational disease that causes ASTHMA-like symptoms. When detected in its early stages, byssinosis is reversible by eliminating exposure to the responsible irritant. When exposure continues the byssinosis can cause permanent damage to the LUNGS with symptoms similar to those of CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). In the United States people who work in jobs where they handle unprocessed cotton have the highest risk of developing byssinosis.

The symptoms of byssinosis tend to be worse at the workplace and improve away from the workplace and typically include wheezing and coughing. The diagnostic path focuses on the work history and includes X-rays of the chest and tests to assess pulmonary capacity and function. The most effective treatment is preventing continued exposure, which may involve workplace improvements or changing jobs. Medications to reduce the HYPERSENSITIVITY REACTION the airways have to the fiber dust, such as bronchodilators and sometimes CORTICOSTEROID MEDICATIONS, can relieve or prevent symptoms. Smoking significantly exacerbates byssinosis, so SMOKING CESSATION is crucial to other treatment approaches.

See also ASTHMA; BERYLLIOSIS; OCCUPATIONAL HEALTH AND SAFETY; SARCOIDOSIS; SILICOSIS.

C–E

chest percussion and postural drainage A therapeutic method for loosening and clearing mucus from the LUNGS, used especially in CYSTIC FIBROSIS and BRONCHIECTASIS, when there is ATELECTASIS, and in other pulmonary disorders in which mucus collects and blocks the flow of air. For this treatment, a respiratory therapist or caregiver trained in the method rhythmically claps, with cupped hands, on the SKIN surfaces of the chest and back over the thoracic cavity with the person receiving the treatment in various postures, depending on the location of the clapping. The therapist may choose to use a mechanized percussor instead of the hands, which allows longer and more intensive percussion.

Clapping over the upper chest (near the collarbones) and upper back (near the shoulder blades) loosens secretions in the upper lobes. Clapping over the midchest (nipple line) and midback loosens secretions in the middle lobes. Clapping over the lower chest (below the nipple line) and lower back loosens secretions in the lower lobes. Precise positioning of the hands when clapping can further target specific segments of the lobes. The percussion of the clapping loosens mucus and secretions within the bronchi, which the person then coughs up to remove from the respiratory tract.

See also COUGH; CYSTIC FIBROSIS AND THE LUNGS.

Cheyne-Stokes respiration A pattern of BREATHING in which periods of APNEA alternate with periods of accelerated breathing. Cheyne-Stokes respiration indicates damage to the brainstem or other NERVOUS SYSTEM mechanisms that regulate breathing. This breathing pattern also occurs in severe HEART FAILURE. During the apneic periods, which may last up to 60 seconds, breathing stops. During the accelerated periods, the RESPIRATORY RATE rapidly increases in rate and depth (hyperpnea) then abruptly stops as the cycle returns to apnea. Cheyne-Stokes respiration may reflect an end-stage (near death) breathing pattern in adults, though may persist for an extended time in people who are comatose.

See also DYSPNEA; TACHYPNEA.

chronic obstructive pulmonary disease (COPD) A serious, often debilitating, and potentially fatal condition in which INFLAMMATION and scarring destroy alveoli, bronchioles, and bronchi. The most common cause of COPD is cigarette smoking; 8 of 10 Americans who have COPD are smokers. Uncontrolled ASTHMA and chronic lung diseases such as ASBESTOSIS and SILICOSIS can also progress to COPD. About 16 million people in the United States have COPD and more than 100,000 of them die from it each year.

COPD takes years to decades to develop, and its damage is permanent. The most common presentation is that of chronic BRONCHITIS, in which there is repeated inflammation of the bronchi. Each bout of inflammation results in the formation of SCAR tissue as the damaged area heals. Over time the scar tissue causes the bronchi to narrow, with areas of constriction that severely limit the flow of air. ATELECTASIS (collapse) may occur in affected bronchial structures, reducing the ability of the lung to diffuse oxygen into the bloodstream.

In about 10 percent of people who have COPD the damage extends to the alveoli, the clusters of air sacs where oxygen–carbon dioxide exchange takes place. Repeated inflammation and scarring causes the alveoli to enlarge and lose elasticity, a state called emphysema. The damaged alveoli can take in air but cannot collapse sufficiently to expel

the air completely. A rare form of emphysema is an inherited deficiency of the enzyme alpha-1-antitrypsin (AAT), which regulates the presence of elastin in the tissues of the alveoli. AAT deficiency results in reduced elastin, further limiting alveolar function. Because of the intimate correspondence between the capillary BLOOD supply and alveolar oxygen content, blood supply shifts away from damaged alveoli.

The ultimate damage of COPD, regardless of whether the primary course of disease started as bronchial or alveolar, is so profound that both dimensions of damage eventually overtake the LUNGS and the lungs lose the ability to recoil (return to their normal shape and size), diminishing the ability to exhale. Consequently, people who have COPD can breathe in with relative ease but struggle to move air back out of their lungs. People who have moderate to advanced COPD typically exhale through pursed lips, an effort to more forcefully exhale. Even with this effort, the person may be unable to blow out a match.

As the disease process progresses the less elastic lungs expand within the thoracic cavity, pushing the ribs out and the DIAPHRAGM down to produce a characteristic barrel chest deformity. However, these structural changes further limit the ability of the diaphragm and intercostal muscles to expand the chest for inhalation, restricting the ability of the lungs to draw in air. This generates a characteristic posture adaptation in which the person leans forward to use other muscles in the neck and shoulders to assist with BREATHING. Ordinary movements such as raising the arms (such as to wash or brush the hair) consequently cause shortness of breath because such movements reduce the involvement of these ancillary muscles. In its later stages COPD affects both inhalation and exhalation.

Symptoms and Diagnostic Path

The symptoms of COPD include

- progressive DYSPNEA (shortness of breath)
- wheezing (whistling sounds with exhalation)
- persistent, productive COUGH
- HEMOPTYSIS (bloody SPUTUM)
- edema (swelling due to fluid retention) in the feet, ankles, and lower legs
- CYANOSIS (bluish hue to the lips and SKIN that signals inadequate oxygenation)
- physical signs characteristic of COPD (barrel chest, purse-lip breathing, forward-leaning posture) when emphysema is dominant
- current or previous cigarette smoking

The diagnostic path includes a complete pulmonary workup to evaluate lung capacity and function, which typically show significant reductions. Chest X-rays and COMPUTED TOMOGRAPHY (CT) SCAN show the extent of damage to the lungs as well as displacement of the thoracic structures. The doctor typically does sputum cultures to identify or rule out INFECTION. Diagnostic blood tests often show an elevated ERYTHROCYTE (red blood cell) count particularly in people who have low oxygen levels, indicative of the body's attempt to improve the oxygen-carrying ability of the blood. Diagnostic efforts focus on ruling out other possible causes for symptoms as well as correlating physical findings with history of smoking.

CLASSIFICATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Classification	Severity	Symptoms
stage 0	at risk	smokes but has no COPD symptoms
stage 1	mild	chronic COUGH
stage 2	moderate	chronic, productive cough DYSPNEA with exertion
stage 3	severe	chronic, productive cough excessive SPUTUM dyspnea at rest right HEART FAILURE common

Treatment Options and Outlook

The most important element of treatment is SMOKING CESSATION. Although it is not possible to reverse damage that has already occurred, treatment aims to minimize further lung damage and improve function of the remaining lung. Medications such as bronchodilators relax and open the airways,

easing the flow of air in and out of the lungs. CORTICOSTEROID MEDICATIONS reduce inflammation and in some people may also help open the airways. When infection is present, the doctor may prescribe ANTIBIOTIC MEDICATIONS. However, people who have COPD often have extensive bacterial flora, making it difficult for the doctor to determine whether there is an actual infection present. People who have COPD should receive annual INFLUENZA immunizations and PNEUMONIA vaccination every five years. As with all lung diseases, it is important to minimize as much as possible other triggers: SINUSITIS, GASTROESOPHAGEAL REFLUX DISORDER (GERD), and exposure to known ALLERGENS.

For some people surgery to remove the upper lobes of the lungs, called lung volume reduction surgery (LVRS), relieves tension within the thoracic cavity and improves pulmonary function and overall lung capacity. LUNG TRANSPLANTATION may be a viable treatment option for some people, replacing one of the diseased lungs with a donor lung. The criteria for these procedures are stringent and take into account numerous health and lifestyle factors.

Nutritional support is essential for people with advanced COPD, who typically lose significant body weight as the effort to breathe requires intense work from numerous muscles. Regular physical exercise is also important. Though breathing with exertion may severely limit the duration of activity, maintaining physical STRENGTH allows the body to make the most of the available oxygen the lungs can diffuse into the bloodstream. Many hospitals have pulmonary rehabilitation programs with specialists who can teach targeted exercises to improve AEROBIC FITNESS and MUSCLE strength. For many people pulmonary rehabilitation is as effective as any surgical alternatives. Walking remains one of the most effective activities.

Complications of COPD are common, particularly in the later stages. Typical complications include HEART FAILURE, PULMONARY HYPERTENSION and RESPIRATORY FAILURE. Doctors sometimes refer to the combination of right-heart failure and pulmonary hypertension as cor pulmonale. People who have COPD are particularly vulnerable to viral infections such as COLDS and influenza, and often develop secondary bacterial infections such as pneumonia and acute bronchitis.

Risk Factors and Preventive Measures

The leading risk factor for COPD is cigarette smoking. The most effective preventive measure is never to smoke and to avoid exposure to secondhand smoke (ENVIRONMENTAL CIGARETTE SMOKE). Smoking cessation can improve lung capacity and function, though cannot undo damage that has already occurred. Prompt and appropriate treatment of other pulmonary conditions, such as asthma, helps minimize permanent damage that could set the stage for COPD to subsequently develop. Though COPD occurs primarily in people over age 40, this is a consequence of cumulative damage to the lungs over time rather than aging.

See also BRONCHITIS; LIVING WITH CHRONIC PULMONARY CONDITIONS; PNEUMOTHORAX; SMOKING AND PULMONARY DISEASE.

collapsed lung See ATELECTASIS.

cystic fibrosis and the lungs An inherited genetic disorder affecting mucus production and clearance, CYSTIC FIBROSIS alters the functioning of exocrine glands throughout the body and affects nearly all of the body's systems. In the LUNGS, cystic fibrosis causes changes in the consistency and composition of the mucus the lungs secrete. The mucus accumulates along the inner walls of the bronchi, causing irritation and INFLAMMATION that eventually thickens the walls of the bronchi. The mucus becomes thick, creating obstructions in the bronchi that reduce air flow and eventually produce regions of ATELECTASIS (collapsed bronchial segments). The plugs of thickened mucus also attract BACTERIA, resulting in recurrent INFECTION that manifest as BRONCHITIS and PNEUMONIA.

Health experts estimate that about 3 percent of the population in the United States carries the recessive GENE MUTATION for cystic fibrosis. The disorder is 5 to 10 times more common among whites than among other racial populations. Even one generation ago, cystic fibrosis typically caused death by late ADOLESCENCE. Current treatment methods and early diagnosis has extended life expectancy into the 30s for most people who have cystic fibrosis, and many live longer. Cystic fibrosis nearly always affects the lungs and requires continuous therapy to maintain adequate BREATHING and oxygenation.

Symptoms and Diagnostic Path

The symptoms of cystic fibrosis vary according to the body system first affected and usually appear in childhood. Chronic productive COUGH, recurrent bronchitis or pneumonia, and pronounced wheezing are among the indications of pulmonary involvement. The diagnostic path includes chest X-rays and pulmonary function tests, which demonstrate changes in lung structure and function characteristic of cystic fibrosis. Other diagnostic procedures look for nonpulmonary indications of cystic fibrosis such as sinus disease, pancreatic disease, decreased BONE DENSITY, and INFERTILITY. Family history of cystic fibrosis provides strong suspicion of the diagnosis. A positive sweat chloride test and GENETIC TESTING that identifies cystic fibrosis mutations. This provides conclusive diagnosis.

Treatment Options and Outlook

Treatment requires close coordination to target symptoms and disease developments across body systems. Pulmonary treatment aims to keep the airways as open as possible and to prevent infection, or treat infection early and aggressively. IMMUNIZATION to protect against CHILDHOOD DISEASES such as PERTUSSIS (whooping cough), CHICKENPOX, and MEASLES are crucial, as are annual INFLUENZA immunizations (flu shots) and pneumonia vaccination every five years at all ages. CHEST PERCUSSION AND POSTURAL DRAINAGE help clear the airways of mucus accumulations. Though coughing is a frustrating symptom, it is also an important function for removing mucus from the chest. Bronchodilators help improve functioning of the airways and removal of mucus from them.

Moderate to high doses of the NONSTEROIDAL ANTI-INFLAMMATORY DRUG (NSAID) ibuprofen (Advil or Motrin) taken regularly may slow bronchial inflammation and damage in many people, especially children. CORTICOSTEROID MEDICATIONS become necessary when ibuprofen can no longer control the inflammation or when inflammation becomes widespread in the lungs. ANTIBIOTIC MEDICATIONS become necessary to treat infections. People who have cystic fibrosis commonly acquire antibiotic-resistant bacteria, which may necessitate treatment with more powerful intravenous antibiotics. Inhaled antibiotic therapies are also becoming available for treatment as well as prophylaxis (prevention).

Cystic fibrosis has numerous nonpulmonary complications that also require close attention. Dysfunction of the PANCREAS results in malabsorption that may necessitate nutritional support. The nature and severity of symptoms vary widely among individuals. Cystic fibrosis is progressive, however, and these treatments are only supportive. When they fail, bilateral LUNG TRANSPLANTATION is the final, though high-risk, treatment option.

Risk Factors and Preventive Measures

The only risk factor for cystic fibrosis is the recessive gene mutation. Because this mutation is relatively prevalent in the American population, many people do not know they carry it until a child develops the disease. Genetic testing and GENETIC COUNSELING may be helpful for people who have family histories of cystic fibrosis.

See also ANTIBIOTIC PROPHYLAXIS; ANTIBIOTIC RESISTANCE; GENETIC DISORDERS; INHERITANCE PATTERNS; ORGAN TRANSPLANTATION.

diaphragm The thin, flat MUSCLE that forms the floor of the thoracic cavity (chest), establishing a physical barrier between the thoracic cavity and the abdominal cavity. Small openings in the diaphragm allow structures such as the AORTA, inferior VENA CAVA, and ESOPHAGUS to pass through. The lower lobes of the LUNGS and the base of the HEART rest against the diaphragm. The diaphragm attaches to the lower ribs and spine in the back, then rises along the back of the ribs to dome forward to form the base of the thoracic cavity. Contraction of the diaphragm tightens this dome, pulling it downward to expand the thoracic cavity. The diaphragm has two equal halves, each called a hemidiaphragm, and is the primary muscle of BREATHING.

Health conditions that can involve the diaphragm include HIATAL HERNIA, in which weakness in the musculature around the esophageal opening allows the stomach to bulge upward through the opening. Hiatal hernia typically causes an uncomfortable burning sensation and may result in regurgitating food or GASTROESOPHAGEAL REFLUX DISORDER (GERD). HICCUPS are muscle spasms of the diaphragm.

THE HEIMLICH MANEUVER

The HEIMLICH MANEUVER, an emergency procedure for ejecting an inhaled object from the TRACHEA, uses the DIAPHRAGM to generate a forceful exhalation. Placing a sharp, upward thrust into the diaphragm causes the diaphragm to rapidly contract and relax, sending its dome higher into the thoracic cavity than usual. The effect strongly compresses the LUNGS, forcing them to propel air outward. The force of the air dislodges the object.

For further discussion of the diaphragm within the context of pulmonary structure and function please see the overview section "The Pulmonary System."

See also BREATHING EXERCISES.

dyspnea Difficulty BREATHING or shortness of breath. There are numerous causes of dyspnea, most of which relate to cardiovascular or pulmonary disorders. Dyspnea occurs when the body does not receive enough oxygen. As oxygen is the fuel for cellular activity, lack of oxygen means cells cannot function properly. When oxygen insufficiency (HYPOXIA) is systemic (involves all the body) the body begins to conserve oxygen for vital uses. This concurrently slows activity of nonessential cells such as skeletal MUSCLE cells and sends signals to the LUNGS and HEART to increase their productivity.

Dyspnea may occur as a result of intense physical activity, such as exercise, in which case it generally diminishes with improved AEROBIC FITNESS. Dyspnea associated with cardiovascular or pulmonary disease may lessen slightly with pulmonary rehabilitation and improved physical conditioning but typically does not improve substantially unless the underlying disease condition improves. CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) and HEART FAILURE are the two most common causes of dyspnea. Doctors assess clinical dyspnea according to the degree to which it interferes with normal activities.

See also APNEA; ASPHYXIATION; DISABILITY AND EXERCISE; INTERSTITIAL LUNG DISORDERS; LIVING WITH CHRONIC PULMONARY CONDITIONS.

emphysema See CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).

GRADES OF DYSPNEA

Grade	Severity	Level of Impairment
grade 1	minimal	shortness of breath with exertion such as climbing multiple flights of stairs, short running such as to catch a bus, or walking uphill
grade 2	mild	shortness of breath with moderate exertion such as climbing a single flight of stairs or walking several blocks on the flat
grade 3	moderate	shortness of breath with mild exertion such as walking one block on the flat; must pause when climbing a single flight of stairs
grade 4	significant	shortness of breath with everyday physical activity; must pause when walking on the flat; must pause every few steps when climbing a flight of stairs
grade 5	incapacitating	shortness of breath with any physical effort including dressing, undressing, showering or bathing; cannot walk more than a few steps without pausing; cannot climb steps

H–I

hemoptysis Bleeding from the LUNGS, which typically manifests through BLOOD in the SPUTUM. Hemoptysis is typically frothy and bright red, though can sometimes be difficult to distinguish from blood that might originate in the ESOPHAGUS or STOMACH.

Hemoptysis that produces a volume of blood greater than the equivalent of two or three teaspoonfuls is a medical emergency that may represent hemorrhage and requires immediate treatment.

Hemoptysis is a symptom of numerous health conditions affecting the lungs, and may appear as blood-streaked sputum or primarily blood with little apparent sputum present. The diagnostic path includes chest X-rays, blood tests, and sputum cultures. Lung hemorrhage is a surgical emergency that generally requires immediate intervention to locate and stop the source of bleeding, commonly a perforated ARTERY. Treatment for less severe bleeding focuses on the underlying cause. The most common cause overall of hemoptysis is BRONCHITIS.

COMMON CAUSES OF HEMOPTYSIS

BRONCHIECTASIS	BRONCHITIS
CYSTIC FIBROSIS	LUNG CANCER
PNEUMONIA	PULMONARY EMBOLISM
TUBERCULOSIS	violent coughing
Wegener's granulomatosis	

See also ANEMIA; GASTROINTESTINAL BLEEDING.

hiccups Dysfunctional or out-of-sequence contractions (spasms) of the DIAPHRAGM. Hiccups generally occur rhythmically in episodes that typically contain four to several dozen contractions. An individual tends to have a personally consistent pattern. Though doctors know the mechanics of hiccups, no one knows what causes hiccups or what, if any, purpose they serve. For most people hiccups are nothing more than an annoyance. However, prolonged attacks can have health consequences.

There is no certain cure for hiccups, though recommended remedies are abundant. Some remedies, such as swallowing a spoonful of sugar or sniffing an ammonia capsule, irritate the airways. Swallowing ice water may activate nerves in the ESOPHAGUS that diffuse the NERVE impulses causing the diaphragm to contract. BREATHING into a paper bag raises the percentage of carbon dioxide in the BLOOD, which alters the brain signals to the diaphragm. It is important that any prospective cure carry little risk of causing harm.

Doctors may treat persistent hiccups with medications that are mildly sedating, such as antiseizure or anticholinergic medications. A mild anesthetic may slow the signals from the brainstem. Mild MUSCLE relaxants and tricyclic antidepressants are also successful in some people. Extended hiccups may result in vasovagal nerve irritation that causes ARRHYTHMIA (irregularities in the heartbeat). In most circumstances of prolonged hiccups, treating underlying health conditions stops the hiccups.

See also HYPERVENTILATION; MYOCLONUS; SPASM.

hyperventilation Rapid, shallow BREATHING that causes carbon dioxide levels in the BLOOD to drop below normal. As the balance between carbon dioxide and other gases in the blood is essential for normal pulmonary and cardiovascular func-

tion, the decrease triggers actions in the body designed to slow the breathing. Key among these is temporary loss of consciousness (fainting), which returns breathing to the involuntary control of the brainstem and restores normal breathing patterns. People who are hyperventilating often feel as if they were not getting enough oxygen, though in fact they are getting plenty. Most often hyperventilation results from emotional stress, panic, or anxiety. Rarely, cardiovascular or pulmonary disturbances cause a similar breathing pattern. Chest X-RAY, blood tests, and ELECTROCARDIOGRAM (ECG) can quickly determine whether this is the case.

The standard treatment for an active episode of hyperventilation is breathing slowly and purposefully. Breathing through only one nostril (holding the other nostril closed with the fingers) helps focus conscious intent on the breathing as well as reduce the amount of air entering the LUNGS.

Though once a common remedy for hyperventilation, BREATHING into a paper bag may allow carbon dioxide levels in the blood to rise too much. Doctors no longer recommend this method.

Once breathing returns to normal the oxygen–carbon dioxide balance in the blood does the same and symptoms such as dizziness or lightheadedness fade. Stress management methods such as MEDITATION and YOGA help lower overall anxiety levels, which reduces hyperventilation episodes. BREATHING EXERCISES are also helpful. Hyperventilation without underlying cardiovascular or pulmonary disease is not harmful to health.

See also HYPOXIA.

hypoxemia See OXYGEN SATURATION.

hypoxia Inadequate oxygen perfusion of the tissues. Hypoxia occurs when the BLOOD cannot deliver adequate oxygen, which may result from pulmonary dysfunction, cardiovascular dysfunction, STROKE, TRAUMATIC BRAIN INJURY (TBI), disorders of the blood such as ANEMIA that affect erythrocytes (red blood cells) or HEMOGLOBIN, and BREATHING disturbances such as APNEA. Hypoxia may involve only a defined organ or area, such as a region of the BRAIN affected by STROKE, or involve the entire body. Permanent tissue damage or tissue death results when hypoxia persists. Symptoms of hypoxia may include CYANOSIS (bluish hue to the lips and SKIN), tiredness, and DYSPNEA (shortness of breath or difficulty breathing). Most hypoxia requires supplemental oxygen with additional treatment that targets the underlying cause.

See also ALTITUDE SICKNESS; DECOMPRESSION SICKNESS; OXYGEN SATURATION; OXYGEN THERAPY; POLYCYTHEMIA VERA.

interstitial lung disorders A broad term for chronic conditions that restrict the ability of the LUNGS to function properly, encompassing more than 150 diseases. Interstitial lung disorders, also called interstitial lung disease as a collective term, are typically obstructive, fibrotic (involve SCAR formation), and progressive. Many arise from occupational exposures such as to asbestos (ASBESTOSIS), silica (SILICOSIS), and coal dust (miner's PNEUMONOCONIOSIS). A variant form that more commonly occurs later in life, idiopathic pulmonary fibrosis (IPF), has no identifiable cause and tends to be more severe in its progression.

The general symptoms, diagnostic paths, and treatment approaches are similar for interstitial lung disorders. Common symptoms include COUGH, DYSPNEA (shortness of breath or difficulty BREATHING), and frequent INFECTION. Treatment targets slowing the progression of the disease, relieving symptoms, and preventing infections. Lung transplantation is sometimes a treatment option for severely progressive IPF. However, many people who have interstitial lung disorders are able to manage their symptoms for years to decades, allowing satisfactory QUALITY OF LIFE.

See also CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD); CYSTIC FIBROSIS AND THE LUNGS; LIVING WITH CHRONIC PULMONARY CONDITIONS.

L–M

Legionnaires' disease A serious and potentially fatal form of PNEUMONIA first identified in 1976 when several hundred people attending a Legionnaires' convention became ill, a number of whom died as a result of the INFECTION. Scientists subsequently isolated the causative bacterium *Legionella pneumophila*. The BACTERIA infect about 18,000 people in the United States each year, about 4,000 of whom die from the disease or its complications. A less severe form of the infection with the same bacteria is Pontiac FEVER, which presents milder forms of similar symptoms (though without subsequent complications). Health experts refer to these infections collectively as legionellosis. Heating and cooling systems in buildings can harbor *L. pneumophila*, which then spread the bacteria through ventilation networks. Frequent and diligent cleaning of these systems is the most effective means for limiting outbreaks of infection.

Symptoms and Diagnostic Path

Legionnaires' disease begins as a typical viral upper-respiratory infection with symptoms that begin 3 to 10 days after exposure and include fever, generalized aches and discomfort, loss of APPETITE, HEADACHE, fatigue, and COUGH. Some people also have gastrointestinal symptoms such as diarrhea. Within a week the symptoms worsen to include coughing up SPUTUM, chest tightness or PAIN, and DYSPNEA (shortness of breath). Some people also experience multiple neurologic symptoms, including confusion and cognitive dysfunction.

A chest X-RAY shows signs of pneumonia, and diagnostic blood tests often show indications of infection in the body. The doctor may order specialized tests to detect the presence of *L. pneumophila* in the sputum or of *L. pneumophila* antigens in the URINE. A key factor in suspecting Legionnaires' disease is knowing the possibility of exposure, either because others have become ill or because the person was at an event at a setting conducive to transmitting Legionnaires' disease, such as a large convention. Other water sources as well as respiratory equipment in hospitals harbor *L. pneumophila,* which has become a common cause of community-acquired pneumonia as well as of NOSOCOMIAL INFECTIONS (hospital-acquired infections).

Treatment Options and Outlook

The primary treatment for Legionnaires' disease is hospitalization for intravenous therapy with the ANTIBIOTIC MEDICATIONS of the macloide or fluoroquinoline class (such as azithromycin or levofloxacin). Illness in some people is mild enough to allow outpatient treatment with oral antibiotics, though others may require hospitalization. As with any severe infection, multiple system failure is a significant risk in people who already have other major health conditions such as CARDIOVASCULAR DISEASE (CVD), DIABETES, or pulmonary disorders. Early diagnosis and treatment are critical; the likelihood of death resulting from the infection increases dramatically when people delay seeking medical care or doctors are unaware of the possibility of the diagnosis. Among people who are otherwise healthy, have normal immune function, and receive prompt treatment, more than 95 percent recover. However, many people continue to have some symptoms, such as fatigue, for several months.

Risk Factors and Preventive Measures

Infection with *L. penumophila* can occur in several venues. People who already have some form of pulmonary compromise, such as ASTHMA or CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD),

seem more likely to contract Legionnaires' disease than people who have healthy lung function with equal exposure to a contaminated source. People who smoke have the highest risk, whether or not they have underlying pulmonary disease. People between the ages of 50 and 70 seem most likely to develop infection after exposure.

The most effective preventive measure is strict maintenance and cleaning of building air-conditioning and heating systems, spas, whirlpools, and other potential sources of culture for the bacteria. Heightened awareness about Legionnaires' disease has resulted in improved diligence. The US Occupational Safety and Health Agency (OSHA) has implemented guidelines for building maintenance. Because the bacteria enter the upper respiratory tract during breathing, there are few personal measures to reduce the risk for infection as often it is not possible or practical to avoid locations that are potential sources of infection.

See also INDOOR AIR QUALITY.

living with chronic pulmonary conditions More than 30 million Americans live with chronic pulmonary conditions such as ASTHMA, CYSTIC FIBROSIS, PULMONARY FIBROSIS, and CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). Though many chronic pulmonary conditions are far more common among people over age 50, chronic pulmonary disease affects young people too. Chronic pulmonary disease requires most people to make accommodations in their lifestyles, recreational activities, and occupations.

Medical Care

People who have chronic pulmonary conditions require ongoing medical surveillance and treatment such that they may feel they "live at the doctor's office." They often take numerous medications and receive respiratory therapy treatments. Many undergo frequent hospitalizations for attacks, exacerbations, and INFECTION. Compliance with medical treatments plan is essential but not always easy. It is common to feel that medications are no longer necessary when they bring about significant improvement, yet taking medications as prescribed is the most effective way to prevent complications and, in many situations, slow or halt the condition's progress.

Self Care

Various lifestyle factors influence the course of chronic pulmonary conditions. Some are actions a person can and should take to improve his or her pulmonary status. Other actions target overall health and well-being. It is important for each person to take leadership of his or her health and care.

Cigarette smoking Cigarette smoking is the most significant factor in many forms of chronic pulmonary disease. The optimal lifestyle choice for healthy lungs is never to start smoking; the next best decision is to stop smoking. Though it is not often possible to undo damage that has already occurred to the LUNGS, smoking cessation can result in improvement no matter when it takes place.

Breathing exercises BREATHING is such a natural occurrence that few people give it a second thought until it becomes a struggle. BREATHING EXERCISES can increase lung capacity and efficiency, teaching ways to get the most from every breath of air.

Nutritious eating habits Working hard simply to breathe requires a lot of calories. For people who have severe pulmonary conditions, breathing can commandeer most of the calories consumed each day. It is important to get enough calories to meet the body's needs and to infuse the body with vital NUTRIENTS that support health and HEALING.

Regular exercise When simply breathing consumes most of the body's energy, it's easy to slack off exercise. Yet the body requires regular physical activity to function at its most efficient. Though chronic pulmonary conditions often limit physical exertion, many activities remain possible with adaptation. Walking is among the most effective exercises, providing AEROBIC FITNESS as well as strengthening muscles. Some people find the relative weightlessness of swimming allows them to do more with less effort. Nearly everyone, regardless of disease type or stage, can engage in small activities that improve the body's fitness. Structured pulmonary rehabilitation programs help people to make the most of the lung function they do have.

Mental health and emotional balance Coping with the challenges and setbacks of chronic health conditions can be overwhelming. Children who have chronic pulmonary conditions may struggle with peer acceptance and feeling left out of school and social activities. Some people find support groups safe ways to express anger, fear, and worry,

as well as to share information and experiences. Other people take comfort in the solitude of prayer or MEDITATION. Stress relief methods such as YOGA and VISUALIZATION help recenter the thoughts and the mind.

Looking to the Future

Though chronic pulmonary conditions are often limiting or debilitating, many people are able to participate in activities they enjoy. With appropriate medical care and self-care, a long and productive life is not only possible but probable for many people who have chronic pulmonary conditions.

See also LIFESTYLE AND HEALTH; QUALITY OF LIFE.

lung abscess A pocket of INFECTION deep within the lung that isolates itself within a defined area of the lung (having a clear boundary between the infected tissue and the healthy tissue), usually behind a blocked segment of BRONCHUS. A lung abscess often follows a known bacterial INFECTION such as PNEUMONIA or BRONCHITIS in which INFLAMMATION or excessive mucus blocks an airway, though may occur without an obvious precipitating infection. A lung abscess may cause COUGH, chest discomfort or PAIN, chills, bouts of profuse sweating (diaphoresis), and difficulty BREATHING (DYSPNEA). Chest X-RAY or COMPUTED TOMOGRAPHY (CT) SCAN allows the doctor to visualize the location and size of the abscess. Cultured SPUTUM samples often provide evidence of the infective PATHOGEN. Treatment with ANTIBIOTIC MEDICATIONS successfully eradicates most lung abscesses. Sometimes the abscess requires drainage, which the doctor often can do by placing a drain through the skin. Occasionally OPEN SURGERY is necessary to open and clean the abscess, and to débride (trim away) damaged or dead tissue surrounding the abscess. Most people heal completely and without complication with appropriate treatment. An untreated lung abscess can result in serious health consequences including significant loss of lung tissue or SEPTICEMIA (total body infection, also called sepsis).

See also ATELECTASIS; BRONCHIECTASIS.

lung cancer Malignant tumors that grow in the LUNGS. Lung CANCER may be primary (originate in the lungs) or metastatic (spread to the lungs from cancer that originates elsewhere in the body). There are two main types of lung cancer: small cell lung cancer (SCLC), which is particularly aggressive, and non–small cell lung cancer (NSCLC). Malignant mesothelioma is a specific kind of cancer that arises from asbestos exposure. Cigarette smoking causes 87 percent of lung cancer in the United States and nearly all SCLC. Other causes of lung cancer include exposure to carcinogenic (cancer-causing) substances such as radon (the second-leading cause of lung cancer) and asbestos (which, when combined with smoking, compounds the risk for lung cancer).

Doctors diagnose 175,000 people with lung cancer in the United States each year. Lung cancer is the leading cause of death from cancer among men and women alike, taking the lives of 160,000 Americans each year and accounting for 30 percent of all deaths from cancer. The five-year SURVIVAL RATE is about 14 percent, which is very low compared to many other kinds of cancer. A key reason lung cancer is so frequently fatal is that it does not show symptoms until it is quite advanced, making treatment difficult. Doctors are able to diagnose only 15 percent of lung cancers when the initial tumor remains localized (confined to a distinct site within the lung), a point in time where intervention could vastly improve the chance of survival.

Non–Small Cell Lung Cancer (NSCLC)

About 80 percent of lung cancer is NSCLC. There are three types of NSCLC:

- ADENOCARCINOMA, which arises from the mucus-secreting cells in the bronchial structures
- squamous cell CARCINOMA, which arises from the epithelial cells that form the inner lining of the airways
- large cell carcinoma, which commonly originates in the bronchi and contains neither squamous cells nor adenomatous (glandular) cells

Staging and treatment protocols are the same across the types of NSCLC. The most common type of NSCLC is adenocarcinoma, which is moderately aggressive. Large cell carcinoma, which accounts for about 20 percent of NSCLC, tends to be more aggressive than other NSCLC tumors and larger and metastasized at the time of diagnosis.

BASIC STAGING OF NON–SMALL CELL LUNG CANCER (NSCLC)

Stage	Extent of Cancer	Treatment Protocols/Options
stage 0	cancer cells are present only in the lining of the bronchi (carcinoma in situ)	surgery or local therapy
stage 1a	tumor is less than 3 centimeters (cm), does not involve a major BRONCHUS, and has not spread beyond the site of origin	surgery (lobectomy) possible adjuvant RADIATION THERAPY
stage 1b	tumor may be more than 3 cm, may have spread to the PLEURA, or partially blocks a bronchus but has not spread to LYMPH NODES	surgery (lobectomy) probable adjuvant radiation therapy
stage 2a	tumor is less than 3 cm and has spread to adjacent lymph nodes but not to the pleura or sites beyond the lung	surgery (lobectomy or pneumonectomy) adjuvant radiation therapy
stage 2b	tumor may be more than 3 cm, may have spread to the pleura, or partially blocks a bronchus and has spread to local lymph nodes alternately, tumor may be of any size and involves the chest wall, mainstem bronchus within 2cm of carina, or causes atelectasis of the whole lung	surgery (lobectomy or pneumonectomy) adjuvant radiation therapy possible adjuvant chemotherapy
stage 3a	tumor may be of any size and involves the chest wall, mainstem bronchus within 2cm of carina, or causes atelectasis of the whole lung extension to mediastinal lymph nodes	radiation therapy and CHEMOTHERAPY in combination possible surgery
stage 3b	tumor may be of any size but there is extensive, unresectable invasion of local structures and/or distant lymph node involvement	radiation therapy and chemotherapy in combination, possibly in preparation for surgery
stage 4	cancer has spread to locations distant from the lung	palliative chemotherapy or radiation therapy supportive care

STAGING OF SMALL CELL LUNG CANCER (SCLC)

Stage	Extent of Cancer	Treatment Protocols/Options
limited	cancer is present in only one lung though may have spread to adjacent LYMPH nodes	CHEMOTHERAPY, possibly in combination with RADIATION THERAPY possibly surgery if small, localized tumor without further involvement possible prophylactic cranial irradiation (PCI)
extensive	cancer is present in both LUNGS, adjacent lymph nodes, and other organs (disseminated disease)	chemotherapy palliative measures to relieve symptoms

The least aggressive of the three types of NSCLC is squamous cell carcinoma, which most commonly occurs as a consequence of cigarette smoking. Some people have more than one type of NSCLC at the time of diagnosis.

Small Cell Lung Cancer (SCLC)

Cigarette smoking causes nearly all SCLC. Small cell lung cancer has a characteristic appearance microscopically, sometimes described as "oat cell." This type of lung cancer grows rapidly and often has metastasized by the time of diagnosis. The outlook (prognosis) for extensive SCLC is particularly poor, with a one-year survival rate of about 20 percent. About 70 percent of people have extensive SCLC at the time of diagnosis.

Malignant Mesothelioma

Malignant mesothelioma is a rare form of cancer that occurs mostly in people who have had exposure to asbestos, particularly those who have ASBESTOSIS (a condition of damage to the lungs resulting from asbestos exposure). Malignant mesothelioma commonly arises from the PLEURA, the membrane that covers the lung. Other mesothelial membranes in the body include the PERICARDIUM, which surrounds the HEART, and the peritoneum, which lines the abdominal cavity. Malignant mesothelioma may also arise from these membranes, though that is less common. Malignant mesothelioma often does not show symptoms until it is well advanced, invading the lungs and adjacent organs or spreading through the LYMPH vessels to sites throughout the body. Doctors diagnose about 2,000 people with malignant mesothelioma each year in the United States and stage it similarly to NSCLC.

NONMALIGNANT MESOTHELIOMA

A noncancerous form of mesothelioma, benign fibrous mesothelioma, may grow from the PLEURA to reach considerable size, compressing inward on the lung or causing PLEURAL EFFUSION. Treatment is surgery to remove the tumor, which cures the condition. Benign fibrous mesothelioma does not spread and does not return after removal, though new tumors may develop in other mesothelial membranes.

Symptoms and Diagnostic Path

Early symptoms of lung cancer are often general and do not point specifically to a pulmonary condition. These early symptoms include

- fatigue
- HEADACHE
- loss of APPETITE and unintended weight loss
- dizziness, confusion, and memory disturbances
- JOINT aches and BONE PAIN
- FEVER without evidence of INFECTION

As the cancer becomes more established and takes over more of the lung, symptoms are more specific. These more specific symptoms include

- persistent COUGH
- HEMOPTYSIS (coughing up bloody sputum)
- chest or back pain
- wheezing (whistling sound with exhalation)
- DYSPNEA (shortness of breath)

The diagnostic path begins with a comprehensive medical examination including chest X-RAY and diagnostic blood tests. The chest X-ray may show an abnormality that, with an appropriate history, would suggest a diagnosis of cancer. Further diagnostic procedures may include COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), POSITRON EMISSION TOMOGRAPHY (PET) SCAN, and lung biopsy, BRONCHOALVEOLAR LAVAGE, or exploratory THORACOTOMY.

A crucial element of diagnosis and treatment planning is staging, which identifies the extent to which the cancer has spread. Doctors may perform additional diagnostic procedures to determine the lung cancer's stage. Non–small cell lung cancer and malignant mesothelioma follow a standard cancer staging scale. Because SCLC is so extraordinarily aggressive it follows a unique staging scale that primarily defines the disease as either limited or extensive.

Treatment Options and Outlook

Treatment options and outlook vary according to the type and stage of lung cancer as well as the person's overall health status. Recommendations

regarding staging and treatment options are prone to change as more research and clinical trials are available. An important part of the approach to managing care is ensuring access to current treatment protocols that may include investigational regimens. Most treatment protocols combine different therapies for optimal effectiveness. Nutritional support during cancer treatment is important to help the body fight the cancer and heal. The available treatments for lung cancer include

- Surgery, which removes the cancerous tumor and portion of the lung that contains it, is the treatment of first choice for NSCLC that remains relatively confined. When the cancer has spread to several locations within the same lung, the surgeon may remove the entire lung (pneumonectomy). Surgery may also be appropriate for very early stage SCLC, though SCLC is rarely found when it remains in an operable stage. The key risks of surgery include bleeding, infection, and limited lung function due to removal of part of the lung. Before surgery the person undergoes evaluation to estimate the ability to function after removal (resection) of part or all of the diseased lung.
- CHEMOTHERAPY, which launches a widespread attack on cancer cells throughout the body, is usually a second-line treatment that follows surgery (except in SCLC, for which it is often the first-line treatment) and may be the primary treatment for cancers that are inoperable or have already metastasized beyond the lungs. Common side effects of chemotherapy include fatigue, MOUTH sores, temporary HAIR loss, and NAUSEA and VOMITING.
- RADIATION THERAPY targets inoperable tumors or follows surgery to eradicate any residual cancer cells after the surgeon has removed the cancer. Radiation therapy may be preventive, as in prophylactic cranial irradiation (PCI) which targets the BRAIN to lower the risk for malignant METASTASES that might form there (the brain is a common metastatic site for lung cancer). Radiation therapy also may be the first-line treatment for limited SCLC or reserved for palliative, directed therapy (such as to treat an obstruction that develops in the lung).
- Photodynamic therapy (PDT) is a technique in which the oncologist administers a light-sensitive DRUG that the cancer cells absorb and then targets the cells with a laser that generates light waves to activate the drug and kill the cells that contain it. PDT may be the primary treatment for small or inoperable tumors, particularly those located in the airways. PDT increases the SKIN's sensitivity to the sun or other sources of ultraviolet light.
- Investigational treatments are available through clinical trials. Oncologists and thoracic surgeons are aware of what trials are ongoing for certain types of cancer or patient profiles and can suggest those that are appropriate. As well the U.S. Institutes of Health's National Cancer Institute (NCI) maintains a current listing of cancer trials, accessible at the NCI's Web site (www.cancer.gov/clinicaltrials). Investigational treatments in the clinical trial stage have shown promise in research studies and are undergoing testing in people. It is essential to fully understand the potential benefits (personal as well as for the treatment of lung cancer in general) and risks of any investigational treatment when considering whether to participate in a clinical trial.

COMMON CHEMOTHERAPY DRUGS FOR TREATING LUNG CANCER

carboplatin	cisplatin	cyclophosphamide
dexamethasone	docetaxel	doxorubicin
etoposide	gemcitabine	ifosfamide
metoclopramide	paclitaxel	teniposide
topotecan	vincristine	vinorelbine

Risk Factors and Preventive Measures

Although not all lung cancer is associated with exposure to cigarette smoke, the vast majority is. In general, were it not for cigarette smoking lung cancer would be rare. This makes lung cancer one of the most preventable forms of cancer because eliminating exposure to cigarette smoke virtually eliminates the likelihood of developing lung cancer. People who smoke are at greatest risk, though people who live in households or work in environments where they continually breathe the smoke from cigarette smokers face nearly as great of a risk. Exposure to asbestos further compounds

the risk for cancer in people who smoke, making any type of lung cancer more likely as well as presenting the specific risk for malignant mesothelioma. The most effective measures for preventing lung cancer are not smoking and avoiding circumstances in which other people are smoking.

Exposure to radon, a naturally occurring gas that comes from the soil and can become concentrated within indoor areas such as homes and office buildings, is the second-leading cause of lung cancer. Radon is odorless and invisible, though radon detectors can measure its presence. The U.S. Environmental Protection Agency (EPA) has established a level of 4 picocuries per liter of air (4 pCi/L) as the maximum acceptable level. Simple ventilation measures can reduce or eliminate radon from indoor air.

See also ADENOMA-TO-CARCINOMA TRANSITION; CANCER PREVENTION; CANCER TREATMENT OPTIONS AND DECISIONS; ENVIRONMENTAL CIGARETTE SMOKE; PAIN MANAGEMENT IN CANCER; RADON EXPOSURE; SMOKING AND CARDIOVASCULAR DISEASE; SMOKING AND PULMONARY DISEASE.

lungs The paired organs in the chest that bring oxygen-bearing air into the body and expel wastes in the form of exhaled gases, primarily carbon dioxide. The right lung has three lobes and the left lung has two lobes. An indentation between the left lung's two lobes, called the cardiac notch, cradles the HEART. The lungs and heart, along with their supporting structures, fill the thoracic cavity (chest). The heart pumps deoxygenated BLOOD to the lungs via the PULMONARY ARTERIES and receives oxygenated blood back from the lungs via the PULMONARY VEINS, circulating the body's entire blood volume through the lungs once every minute.

The TRACHEA (windpipe) carries air from the THROAT into the lungs, branching into the right and left BRONCHUS to deliver air to the right and left lung, respectively. Each bronchus further subdivides into mainstem bronchi going to each lobe of the lung and into progressively smaller bronchial branches within the lungs. The smallest branches are the bronchioles which terminate in the alveoli, grapelike clusters of tiny sacs where the OXYGEN–CARBON DIOXIDE EXCHANGE takes place. A weblike mesh of capillaries (tiny blood vessels) covers each ALVEOLUS. Each lung contains about 300 million alveoli, which gives lung tissue a spongelike appearance.

Each lobe of the lung consists of multiple segments, anatomically and physiologically distinct. A bronchial structure—bronchi, bronchioles and alveoli along with supporting nerves, arteries, and veins—supplies each segment. The three lobes of the right lung contain 10 segments; the two lobes of the left lung contain 8 segments. This structural and functional compartmentalization aids the efficiency of the lung as well as helps protect it in the event of injury (either traumatic or due to disease), enabling portions of the lung to function when others are damaged or diseased.

Lung tissue contains elastin, a substance that, as the name implies, gives the lung tissue elasticity. The lungs have no ability to move on their own but rather function as a pair of synchronized bellows that stretch and rebound with contraction and relaxation of the DIAPHRAGM and the intercostal muscles (the muscles between the ribs). Contraction of these muscles expands the chest, and the lungs stretch to fill the space which pulls air into the lungs. When these muscles relax, the chest returns to its normal size and the lungs rebound, pushing air back out of the lungs. Each combination of inhalation and exhalation constitutes a RESPIRATORY CYCLE. The lungs complete 15 to 20 respiratory cycles each minute in a healthy adult.

HEALTH CONDITIONS THAT AFFECT THE LUNGS

ASBESTOSIS	ASPERGILLOSIS
ASTHMA	ATELECTASIS
BERYLLIOSIS	BRONCHIECTASIS
BRONCHITIS	BYSSINOSIS
CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)	CYSTIC FIBROSIS
LUNG ABSCESS	LEGIONNAIRES' DISEASE
PNEUMOCONIOSIS	LUNG CANCER
PNEUMONITIS	*Pneumocystis carinii*
PULMONARY EMBOLISM	PULMONARY EDEMA
PULMONARY HYPERTENSION	PULMONARY FIBROSIS
TUBERCULOSIS	SILICOSIS

Oxygen–carbon dioxide exchange, the process of getting oxygen into and removing carbon dioxide from the blood, is the primary purpose of the lungs and is a function of physics in which mole-

cules follow the path of least resistance. During inhalation the air pressure within the alveoli is less than the air pressure outside the lungs. Oxygen molecules pass across the thin alveolar membrane and into the capillaries to enter the bloodstream. During exhalation the air pressure within the alveoli is greater than the atmospheric air pressure, inducing carbon dioxide molecules to cross from the capillaries into the air in the alveoli.

For further discussion of the lungs within the context of pulmonary structure and function please see the overview section "The Pulmonary System."

See also EPIGLOTTIS.

lung transplantation An OPERATION to replace an individual's diseased lung with a healthy donor lung. Doctors performed the first successful lung transplantation in 1983 and now perform several hundred lung transplantations each year. A lung transplantation may involve one lung or both LUNGS. Less commonly a lung transplantation includes both lungs and the HEART, such as to treat primary PULMONARY HYPERTENSION with HEART FAILURE.

Donor lungs come primarily from people who donate their organs upon death. Live lobular donation, in which a living donor undergoes surgery to have a lobe of the lung removed for transplantation (lobectomy), is occasionally a viable option for people who can find a tissue match among two prospective donors (usually family members) willing and medically capable of donating a healthy lung lobe (live lobular donation typically requires two lobes). Doctors most commonly consider living lobular donation as an option for children who have aggressive CYSTIC FIBROSIS.

Many circumstances influence whether an individual is an appropriate candidate for lung transplantation. Because donor lungs are in short supply, the criteria for transplantation are stringent though vary somewhat among transplant centers. In general, lung transplantation recipients must be under age 65, in good health except for their pulmonary conditions, and demonstrate willingness and ability to comply with the post-transplantation care regimen. Transplantation criteria nearly always exclude people who have cancer (lung or other), immunodeficiency disorders, active TUBERCULOSIS, neurologic or neuromuscular disorders, LIVER disease, or renal (kidney) disease.

CONDITIONS FOR WHICH LUNG TRANSPLANTATION IS AN OPTION

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)	CYSTIC FIBROSIS
bronchiolitis	BRONCHIECTASIS
primaryPULMONARY HYPERTENSION	alpha-1-antitrypsin deficiency
PULMONARY FIBROSIS	SARCOIDOSIS

Surgical Procedure

The operation for performing a lung transplantation is a THORACOTOMY, done with the person under general ANESTHESIA. The surgery generally takes three to six hours to complete. Typically one surgical team removes and prepares the donor lung and another surgical team removes the diseased lung from the person receiving the lung transplantation. A donor lung remains viable for only four to six hours. Most people are on CARDIOPULMONARY BYPASS during the surgery, though advances in surgical techniques are reducing the need for this. MECHANICAL VENTILATION during recovery and for up to 72 hours after surgery is common. A lung transplant recipient typically stays about 10 days in the hospital after the surgery, the first three to five of them in the intensive care unit (ICU). Recuperation and return to daily activities takes about three to five months for most people.

Risks and Complications

The most significant risk of lung transplantation is rejection of the transplanted lung. This risk is highest during the first four weeks after the surgery and remains a perpetual threat. The risk of death, usually resulting from acute organ rejection, is highest during the first year after the transplant. People who receive organ transplants must take IMMUNOSUPPRESSIVE THERAPY for the remainder of their lives. These medications block the IMMUNE SYSTEM from perceiving the transplanted organ as foreign and attacking it. Immunosuppressive therapy increases the risk for INFECTION. Infections such as INFLUENZA or PNEUMONIA can be life-threatening for people with organ transplants; most transplant programs require organ recipients to agree to receive annual immunizations to help protect

against these infections among their criteria for accepting recipients. Long-term immunosuppression carries numerous risks, including a significantly increased likelihood for developing LYMPHOMA, a cancer of the LYMPH structures.

A major complication that affects up to 50 percent of lung transplant recipients is bronchiolitis obliterans, a condition in which the bronchioles (the smallest airways in the lungs) become inflamed and then fibrotic. The fibrotic (SCAR) tissue blocks the narrow openings of the bronchioles, preventing air from reaching the alveoli. As greater numbers of bronchioles become involved, pulmonary function deteriorates. Bronchiolitis is itself an indication for lung transplantation. CORTICOSTEROID MEDICATIONS can help limit the INFLAMMATION though cannot prevent the condition from developing or progressing.

Outlook and Lifestyle Modifications

Most people who receive transplanted lungs can return to many of their regular activities, including physical exercise, with few restrictions unless complications develop. It is important to avoid cigarette smoke and other substances that may irritate or inflame the lungs, and to minimize exposure to other people who have viral or bacterial infections such as sore throats and other common illnesses. Lung transplantation requires regular medical care for follow-up and evaluation of pulmonary function and lung health, with immediate treatment for potential problems and complications. About 45 percent of people who undergo lung transplantation live five years or longer with their donor lungs.

See also HEART TRANSPLANTATION; ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

mechanical ventilation A method for providing assisted respiration to an individual whose LUNGS cannot maintain respiratory support on their own (RESPIRATORY FAILURE). During mechanical ventilation, a machine (the ventilator) rhythmically pushes air into the lungs through an endotracheal tube or TRACHEOSTOMY tube. An endotracheal tube is a flexible plastic tube inserted through the NOSE or MOUTH into the TRACHEA, with an inflatable cuff that holds it in place. A tracheostomy tube enters the trachea through an incision in the neck, bypassing the upper airways (including the mouth and throat). The lungs continue to do the work of OXYGEN–CARBON DIOXIDE EXCHANGE.

Mechanical ventilation may provide full respiratory support, in which BREATHING occurs only with the ventilator's function, or partial respiratory support, in which the ventilator functions only when the person's natural breathing is insufficient. As with normal respiration the inhalation phase of the RESPIRATORY CYCLE is active, with the ventilator sending air under pressure into the lungs, and the exhalation phase is passive, with the ventilator allowing the thoracic cavity's relaxation to expel air. The ventilator typically utilizes continuous POSITIVE AIRWAY PRESSURE (CPAP), which keeps the trachea, bronchi, and bronchioles from collapsing.

There are numerous applications for, and varying levels of, mechanical ventilation. Temporary mechanical ventilation is customary after major cardiovascular or pulmonary operations and during recovery from major trauma. Other circumstances in which mechanical ventilation is a therapeutic option include

- high-level (cervical and upper thoracic) SPINAL CORD INJURY that affects the nerves regulating contraction of the DIAPHRAGM and intercostal muscles (the muscles of breathing)
- injury to the respiratory centers of the BRAIN and brainstem
- degenerative neurologic conditions that affect respiratory function
- increased respiratory demands that exceed the lungs' ability to deliver, such as in severe infections

The ventilator is primarily a mechanized bellows that fills with air (and supplemental oxygen if necessary) that inflates the lungs using positive pressure. The doctor determines the RESPIRATORY RATE, air volume (amount of air the ventilator delivers), and flow pressure (pressure under which the ventilator delivers air to the person). In some situations the person does not need help with breathing but just needs an endotracheal tube or tracheostomy to protect the airway and minimize the risk of aspirating foreign matter into the lungs. In such a situa-

tion the tube may connect only to an oxygen source without a ventilator.

THE IRON LUNG

One of the first mechanical ventilators was nicknamed the iron lung. This device, which used a vacuum pump within a sealed chamber to cause the chest to rise, debuted during the POLIOMYELITIS epidemics of the 1930s and 1940s. Though cumbersome (it encased the person from toes to neck), the iron lung saved countless lives.

Complications of short-term mechanical ventilation are usually minor and may include sore throat (from the endotracheal tube) and INFECTION. Infection is a greater risk with long-term mechanical ventilation, with PNEUMONIA being the most common. The longer a person receives mechanical ventilation, the more difficult it becomes to wean the person to breathe independently. Long-term mechanical ventilation becomes an element of life support, which raises questions of QUALITY OF LIFE. Doctors encourage adults to establish advance directives to help guide life-support decisions.

See also ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS); CARDIOPULMONARY BYPASS; OXYGEN SATURATION.

middle lobe syndrome See ATELECTASIS.

oxygen–carbon dioxide exchange The process by which oxygen passes from the air in the LUNGS to the HEMOGLOBIN in the BLOOD, and carbon dioxide from the hemoglobin passes into the air in the lungs. Oxygen–carbon dioxide exchange is fundamental to life and is the primary function of the lungs. Oxygen–carbon dioxide exchange takes place between the alveoli, the tiny bubblelike sacs deep within the lungs, and the capillaries, the tiniest blood vessels of the cardiovascular system. The membranous tissue of an ALVEOLUS is only one cell or two cells in thickness. A mesh of capillaries encloses each of the 300 million or so alveoli in the lungs. The walls of the capillaries are also only one cell in thickness. Some disease states cause this interface to thicken, thus making the oxygen–carbon dioxide exchange ineffective.

Oxygen and carbon dioxide molecules (as well as the molecules of other gases such as nitrogen and highly toxic carbon monoxide) can easily pass through the walls of the alveoli and the capillaries, moving in the direction of least resistance. Oxygen molecules move from the alveoli into the capillaries with inhalation. Hemoglobin molecules in the erythrocytes (red blood cells) attract the oxygen molecules, binding with them to carry them through the bloodstream. At exhalation carbon dioxide molecules cross the alveolar membrane to join the gases within the alveoli. Exhalation expels the carbon dioxide into the atmosphere.

Factors that influence oxygen–carbon dioxide exchange include the concentration of oxygen in the air, which is about 21 percent at sea level and decreases with elevation.

Numerous pulmonary conditions affect oxygen–carbon dioxide exchange. Infections such as INFLUENZA and PNEUMONIA can cause the alveoli to fill with fluid, blocking air from reaching the alveolar membranes. Inhaled substances, notably cigarette smoke, can clog small bronchioles, preventing air from reaching the alveoli. Eliminating their causes usually reverses most if not all of these circumstances to restore full function (though damage resulting from long-term cigarette smoking or repeated pneumonia can become permanent). Conditions that cause scarring (fibrosis), such as CYSTIC FIBROSIS, SARCOIDOSIS, PNEUMOCONIOSIS, and untreated TUBERCULOSIS, block air from reaching the alveoli. ATELECTASIS and BRONCHIECTASIS are collapses of lung segments that also block the movement of air into the deep lung tissues. Conditions in which the alveoli rupture and form enlarged sacs, such as alpha-1-antitrypsin deficiency (an inherited genetic disorder), destroy the surface area and reduce the effectiveness of the gas exchange. Both late-stage CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) and early emphysema-predominant COPD cause scarring and alveolar rupture. Such structural damage is permanent.

See also CYSTIC FIBROSIS AND THE LUNGS; LUNG TRANSPLANTATION; OXYGEN SATURATION; OXYGEN THERAPY.

oxygen saturation The percentage of HEMOGLOBIN molecules in the BLOOD that are bound to oxygen molecules. Normal oxygen saturation of the arterial blood is 96 to 98 percent. Saturation significantly below normal, for instance 88 percent, indicates RESPIRATORY FAILURE and may be life-threatening. Oxygen saturation is an essential measurement for assessing cardiovascular and pulmonary effectiveness. Inadequate oxygen saturation in the blood is hypoxemia.

The primary method for measuring oxygen saturation is pulse oximetry, which is painless and noninvasive. The pulse oximeter consists of two

components, an emitter and a tiny computer chip. The emitter is a small device that fits over the fingertip or on the EAR lobe. It projects beams of red and infrared light, which pass through the tissue to a sensor on the other side. The volume of blood in the tissue at systole (peak contraction of the HEART) is greater, resulting in more light being absorbed than with the lesser volume of blood in the tissue at diastole (relaxation of the heart). The oximeter's computer chip measures this difference and uses it to mathematically calculate the percentage of oxygen the hemoglobin carries.

See also OXYGEN–CARBON DIOXIDE EXCHANGE; OXYGEN THERAPY.

oxygen therapy The administration of oxygen via nasal cannula, face mask, endotracheal tube (tube inserted into the THROAT), or transtracheal catheter (small tube surgically placed through the outside of the throat into the TRACHEA). Oxygen therapy delivers oxygen at a percentage higher than that of normal air, which is 21 percent oxygen at sea level. Oxygen therapy can deliver oxygen from about 25 percent to 100 percent. This boosts the OXYGEN SATURATION of the BLOOD, which becomes necessary when the LUNGS cannot adequately diffuse oxygen into the blood or the HEART cannot circulate oxygenated blood at a level that meets the body's needs.

Oxygen is highly flammable. Do not smoke, have an open flame, or use electrical appliances (including extension cords) in the vicinity of the oxygen supply.

Because 100 percent oxygen can be harmful to body tissues, doctors administer this level of oxygen therapy only to treat respiratory crisis. Supplemental oxygen therapy may be an element of treatment for cardiovascular conditions such as ISCHEMIC HEART DISEASE (IHD) and HEART FAILURE as well as pulmonary conditions such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), PNEUMONIA, severe ASTHMA, and ATELECTASIS.

In the hospital setting the oxygen supply is centralized, with access ports in patient care areas. Oxygen-delivery tubing plugs into the port, with an individualized flow regulator to adjust the percentage of oxygen. Oxygen tanks for home oxygen therapy contain compressed or frozen (liquid) oxygen, with flow regulators and often a device that releases oxygen only on inhalation. Home oxygen therapy may use an oxygen concentrator instead of supplemental oxygen. An oxygen concentrator extracts nitrogen from room air to increase the air's concentration of oxygen. Oxygen concentrators can deliver oxygen only at low flow rates, however, making them useful only for people who require minimal oxygen supplementation. It is important to have adequate supplemental humidification as well during oxygen therapy, as the higher concentration of oxygen is drier than environmental air. Oxygen therapy may be short-term or long-term treatment, depending on the condition that causes its use. The person may also use oxygen therapy continuously, only during sleep, or only during physical activity depending on his or her underlying disease and respiratory needs.

OXYGEN THERAPY

Oxygen Therapy Device	Percentage of Oxygen
nasal cannula	25 to 40 percent
face mask	30 to 50 percent
nonrebreathing mask	50 to 90 percent
transtracheal catheter	up to 100 percent
endotracheal tube	up to 100 percent
bag and mask resuscitator	up to 100 percent

See also OXYGEN–CARBON DIOXIDE EXCHANGE; TRACHEOSTOMY.

P

pleura The membrane that covers the exterior surface of the LUNGS and lines the inside of the thoracic cavity. The pleura has the consistency of wet tissue paper and appears to cling to the lungs. The pleural space (thin area between the two layers of pleura) protects the lungs from contact with other structures within the thoracic cavity, and contains a very small amount of fluid that reduces friction with BREATHING. The pleural space can become irritated, inflamed, and infected, causing conditions such as PLEURISY and PLEURAL EFFUSION.

For further discussion of the pleura within the context of pulmonary structure and function please see the overview section "The Pulmonary System."

See also ALVEOLI; BRONCHUS; INFECTION; INFLAMMATION; THORACIC DUCT; TRACHEA.

pleural effusion An increase in the amount of fluid between the PLEURA. In health there is a very small amount of fluid, only 10 to 20 milliliters, within the pleural cavity. A pleural effusion can contain upward of 2 liters of fluid, though much smaller quantities (less than 400 milliliters) are more common. Pleural effusion compresses the LUNGS, preventing them from fully expanding. Many conditions can cause pleural effusion. Pleural effusion is exudative when it results from INFLAMMATION of the pleura (PLEURISY). Pleural effusion is transudative when pressure changes in the body's fluid balance (osmotic) mechanisms allow more fluid to cross the pleural membrane such as with HEART FAILURE. A hemothorax exists when the excess fluid is BLOOD, and a chylothorax occurs when the excess fluid is LYMPH.

Many people who have pleural effusion have no symptoms. When present, symptoms include

- DYSPNEA (shortness of breath or difficulty BREATHING)
- CHEST PAIN, primarily with inhalation
- fatigue or weakness

The diagnostic path typically includes chest X-RAY, COMPUTED TOMOGRAPHY (CT) SCAN or ULTRASOUND, and THORACENTESIS (withdrawing a sample of the fluid using a syringe with a large needle). Treatment aims to reduce the volume of fluid as well as identify the underlying cause (such as infection). Thoracentesis may also be therapeutic, allowing the pulmonologist to drain away the excess fluid. Doctors generally drain no more than 1.5 liters of fluid at a time because more substantial withdrawal can result in rapid fluid shifts, causing cardiovascular instability and the development of pulmonary edema (fluid accumulation in the lung tissue). Recovery depends on the condition causing the pleural effusion.

See also LUNG CANCER; PULMONARY EDEMA.

pleurisy INFLAMMATION of the PLEURA, also called pleuritis. Pleurisy can develop as a consequence of direct irritation or INFECTION in the pleural space, or as a consequence of infection or INFLAMMATION involving the LUNGS such as TUBERCULOSIS or PNEUMONIA. AUTOIMMUNE DISORDERS can cause inflammation, such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) and SARCOIDOSIS. The characteristic symptom of pleurisy is sudden, sharp, and often severe PAIN during inhalation and exhalation that subsides with holding the breath. The pain may occur on only one side of the chest or both sides, and may feel as though it comes from the back or under the shoulder blades, depending on the site of the inflammation. Some people also have a persistent, dry COUGH.

Upon AUSCULTATION with a STETHOSCOPE the doctor can hear an abnormal abrasive sound called a pleural rub, which is the sound of the irritated layers of the pleura rubbing against each other. Chest X-RAY confirms whether there is PLEURAL EFFUSION in which the pleural cavity contains excessive fluid. The doctor may also choose to do an ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN of the thorax.

Treatment targets any underlying cause, when identified. For simple pleurisy, treatment is usually NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve inflammation and pain. The doctor may also prescribe a cough medicine to control coughing. Most people cover fully and uneventfully from an episode of pleurisy. People who have chronic pulmonary conditions or who smoke may have recurrent pleurisy, which can result in long-term thickening or scarring of the pleura.

See also BRONCHITIS; PERICARDITIS; PNEUMONITIS; SMOKING AND HEALTH.

pneumoconiosis The collective term for pulmonary conditions that result from occupational exposure to dust and fiber irritants. The conditions result in the same end-stage disease, pulmonary fibrosis, though follow different patterns of progression, depending on the substance and exposure patterns. The primary forms of pneumoconiosis that occur in the United States are

- ANTHRACOSIS, also called coal worker's pneumoconiosis (CWP) and black lung disease, which results from inhalation of coal dust
- ASBESTOSIS, which results from inhalation of asbestos fibers and dust
- BERYLLIOSIS, which results from inhalation of beryllium dust
- BYSSINOSIS, also called brown lung and cotton bract disease, which results from inhalation of raw cotton fibers and dust
- SILICOSIS, which results from inhalation of silica dust

U.S. occupational health experts and federal agencies began tracking and reporting deaths due to pneumoconiosis in 1968, as data related to occupational health. The federal Coal Mine Health and Safety Act of 1969, which established levels of dust exposure standards, was the first substantial effort in the United States to reduce such deaths. The Black Lung Act of 1972 further acknowledged the significant occupational health problems of coal workers, expanding the regulatory scope of the 1969 legislation and establishing a program of government-funded health care for coal workers who developed anthracosis (called black lung disease in the legislation and regulations).

Federal regulation controls occupational exposure to other sources of pneumoconiosis, notably silica, as well. Health experts attribute the declining numbers of diagnoses and deaths in all pneumoconioses, except asbestosis, largely to such controls. The number of people diagnosed with and who die from asbestosis continues to climb, however, because the time between exposure and illness is a minimum of 20 years. Regulatory changes will benefit workers who began working in affected occupations in the last decades of the 20th century, though health experts anticipate that asbestosis will keep rising among those whose work history predates regulations as their average age increases. Peak exposure to asbestos in the United States occurred in 1975, according to the U.S. Centers for Disease Control and Prevention (CDC), so health experts expect asbestos-exposure related illness to peak between 2015 and 2020. However, asbestos exposure in general dropped significantly after the late 1970s when federal legislation restricted the use of asbestos in materials such as building insulation, ceiling tiles, and flooring.

The other key factor contributing to diminishing disease and death rates for pneumoconiosis is the declining numbers of people working in occupations where exposure is a hazard. The number of coal miners in the United States dropped by half between the 1980s and the 1990s, for example, as more mining functions have become automated or mechanized. Automation continues to reduce hazardous occupational exposures in most industries.

Symptoms and Diagnostic Path

Dry, nonproductive COUGH and DYSPNEA (shortness of breath), particularly with exertion, are the key symptoms of most forms of pneumoconiosis. Anthracosis, berylliosis, byssinosis, and silicosis

FORMS OF PNEUMOCONIOSIS

Form of Pneumoconiosis	Causative Substance	Occupational Exposure
anthracosis	coal dust	coal mining
asbestosis	asbestos fibers and dust	insulation, aerospace components, brake lining, shipbuilding
berylliosis	beryllium dust	electronics, aerospace manufacturing, metal working, metal reclamation processing
byssinosis	raw cotton fibers and dust	raw cotton processing, textile production
silicosis	silica dust	sandblasting, sand and gravel mining

may show symptoms after relatively short periods of exposure and often improves when exposure ceases. Asbestosis may develop after relatively short exposure though symptoms typically do not become apparent for decades after exposure. The diagnostic path focuses on occupational history and exposure patterns. Diagnostic examination typically includes AUSCULTATION, chest X-RAY, pulmonary function tests, and imaging procedures such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI). The pulmonologist may also perform BRONCHOSCOPY, BRONCHOALVEOLAR LAVAGE, or lung biopsy to rule out other causes of symptoms.

Treatment Options and Outlook

The first and most important element of treatment is to end the exposure. Nearly all forms of pneumoconiosis improve with this measure. Permanent damage to the lungs that has already occurred, such as fibrosis, does not reverse though its progression may stop. The disease process of asbestosis is such that damage continues long after exposure ceases. The outlook depends on the form of pneumoconiosis, the length or extent of exposure, and whether the person also smokes. Cigarette smoking significantly worsens both the disease process and the outlook.

Risk Factors and Preventive Measures

Occupational pneumoconiosis develops with exposure to substances that enter and remain in the lungs. Avoiding such exposure is the only certain means of prevention. Workplace measures to reduce exposure to the lowest possible levels include environmental controls to filter or otherwise contain dusts and fibers. Personal protective equipment may include clothing, masks, and respirators.

See also ASTHMA; BRONCHITIS; CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD); INDOOR AIR QUALITY; OCCUPATIONAL HEALTH AND SAFETY.

pneumonectomy See THORACOTOMY.

pneumonia INFLAMMATION of the LUNGS, usually the result of an INFECTION, that causes the alveolar sacs to fill with fluid or pus. Pneumonia is the most serious consequence of INFLUENZA, and in combination with influenza is the seventh leading cause of death in the United States. Pneumonia may be lobar, affecting the entire lobe of the lung, or bronchial, affecting diffuse areas of lung. The more of the lung that is involved, the more serious the consequences. People most vulnerable to infection resulting in pneumonia and complications from pneumonia are the very young, the very old, and those who have immunodeficiency disorders such as HIV/AIDS or other serious health conditions such as CANCER. About two million people in the United States develop pneumonia each year, and about 60,000 die as a result of the infection or its complications.

Pathogens that can cause pneumonia include viruses, BACTERIA, and fungi. The pneumonias that result from these pathogens are contagious—that is, an infected person can pass them to others through sneezing and coughing. SPUTUM (mucus and debris from the respiratory tract) contains the infective agent. Pneumonia also can develop after exposure to bacteria aspirated into the lungs (such as in a person who is weak and vomiting). Nosocomial pneumonias develop from pathogens common in environments such as hospitals and skilled nursing facilities and infect people who are already weak as a result of other health conditions (especially those who are IMMUNOCOMPROMISED).

Viral Pneumonia

A number of viruses can cause pneumonia, the most common of which are influenza A, influenza B, parainfluenza, respiratory syncytial VIRUS, ADENOVIRUS, varicella-zoster virus, EPSTEIN-BARR VIRUS, and coxsackievirus. CYTOMEGALOVIRUS (CMV) pneumonia can develop in people who are IMMUNOCOMPROMISED. ANTIVIRAL MEDICATIONS are available for some of these viral infections and can shorten the course of the infection and lessen the severity of symptoms. Most otherwise healthy people recover fully from viral pneumonia. Bacterial pneumonia may develop secondarily to viral pneumonia.

Bacterial Pneumonia

Pneumonia in people over age 30 is more likely to result from bacterial infection than other causes. *Staphylococcus aureus, Haemophilus influenzae* type b (Hib), *Chlamydia pneumoniae*, and *Streptococcus pneumoniae* are the strains of bacteria most commonly responsible for bacterial pneumonia. *S. pneumoniae* causes the most common form of bacterial pneumonia, pneumococcal pneumonia, which often follows a viral infection of the upper respiratory tract. Hib pneumonia, despite the bacterium's name, has nothing to do with the influenza virus and affects primarily young children. Hib vaccination has nearly eliminated this type of pneumonia among children in the United States. *S. aureus* tends to be opportunistic and accounts for about 20 percent of nosocomial pneumonia. ANTIBIOTIC MEDICATIONS are necessary to treat bacterial pneumonia. Even with antibiotic therapy, however, bacterial pneumonia is a serious illness that can be deadly among the very young and the very old.

Mycoplasmal Pneumonia

Mycoplasma are tiny organisms related to bacteria, commonly called atypical bacteria. The pneumonia they cause is typically mild though tends to linger. A common nickname for mycoplasmal pneumonia as "walking pneumonia" because its symptoms are enough to make people feel unwell though usually not enough to interrupt regular activities. Most people recover without treatment, though antibiotics usually speed recovery. COUGH and HEADACHE may persist for several weeks.

Fungal Pneumonia

Fungi may cause pneumonia in people who take antibiotics for an extended period of time, as antibiotics suppress the NORMAL FLORA (normally present bacteria) that otherwise keep fungi in check. Fungal pneumonias are rare but when invasive in someone who is immunocompromised, they can be life-threatening.

Pneumocystic Carinii Pneumonia

Pneumocystis carinii is an opportunistic pneumonia that occurs nearly exclusively in people who are immunocompromised, including those who have HIV/AIDS, are receiving IMMUNOSUPPRESSIVE THERAPY following organ transplantation, or are undergoing chemotherapy for cancer treatment. During the early days of the AIDS epidemic, *P. carinii* pneumonia was often the first indication that a person had HIV/AIDS. Doctors may prescribe prophylactic ANTIFUNGAL MEDICATIONS for people at risk for *P. carinii* pneumonia. Such prophylaxis has now made *Pneumocystic* pneumonia a relatively rare event in people whose HIV infection is well-managed.

Symptoms and Diagnostic Path

The symptoms of pneumonia vary somewhat with the type of pneumonia, though commonly include

- cough that produces greenish yellow sputum or HEMOPTYSIS (bloody sputum)
- FEVER (sometimes high)
- chills or sweating

- generalized discomfort and aches
- fatigue
- chest discomfort or PAIN, especially with inhalation
- DYSPNEA (shortness of breath) or TACHYPNEA (rapid BREATHING)

Symptoms may develop gradually or come on suddenly. Though the pattern of the symptoms provides good clues as to the cause of the pneumonia, the doctor cannot determine whether the infection is viral or bacterial without sputum or blood tests. Viral pneumonia does not respond to antibiotic therapy, though a good number of people who have viral pneumonia develop secondary bacterial pneumonia that does require antibiotics. The diagnostic path typically includes chest X-ray, which shows the areas of infiltration (fluid or pus accumulation) within the lungs. Other factors that help determine the kind of pneumonia include knowledge of local or regional outbreaks of viral or bacterial pneumonia, history of recent upper respiratory infection or influenza, and the presence of other health conditions such as HIV/AIDS. Sputum culture may also help in the diagnosis although most viruses and atypical bacteria do not readily grow in culture.

Treatment Options and Outlook

Treatment depends on the cause of the infection and may include antibiotics for bacterial pneumonia, antiviral medications or management of symptoms for viral pneumonia, and antifungal medications for fungal pneumonia. Because secondary bacterial pneumonia can develop as a complication of other types of bacteria, symptoms that fail to improve within 10 days or that worsen require further medical evaluation. Most people who are otherwise healthy make full recovery from pneumonia, though may take six to eight weeks to feel back to normal.

Risk Factors and Preventive Measures

The very young, the very old, and those who have serious health conditions of any kind are at greatest risk for pneumonia. Health experts recommend annual influenza IMMUNIZATION and pneumococcal vaccination for people who have such risks. Diligent HAND WASHING and conscientious cough and SNEEZE precautions help reduce the spread of infectious agents. Early diagnosis and appropriate treatment reduce the likelihood of complications.

See also ASPERGILLOSIS; CHEST PAIN; LEGIONNAIRES' DISEASE; NOSOCOMIAL INFECTIONS.

pneumonitis INFLAMMATION of the LUNGS resulting from exposure to an irritant. The inflammation causes the airways to narrow and to increase mucus secretion, reducing the pathways for the flow of air. The major types of pneumonitis are

- aspiration pneumonitis, which develops when foreign matter, such as vomitus or water, enters the airways and lungs
- chemical pneumonitis, which results from inhaling toxic fumes
- hypersensitivity pneumonitis, which is an IMMUNE REACTION to an inhaled substance
- radiation pneumonitis, which occurs as a SIDE EFFECT of RADIATION THERAPY to the chest and lower neck, such as to treat LUNG CANCER, THYROID CANCER, or BREAST CANCER

The primary symptoms of pneumonitis are persistent COUGH and DYSPNEA (shortness of breath). The doctor makes the diagnosis on the basis of the history of the symptoms, including when they began, what circumstances existed, and in particular any known or suspected exposures that occurred. Near drowning, for example, may result in aspiration of water. SWALLOWING DISORDERS may allow food or drink to enter the airways. Chemical pneumonitis and hypersensitivity pneumonitis often result from occupational exposures (and sometimes exposure to pets such as birds) and may indicate the early stages of pulmonary disease related to exposures such as to dusts and fibers. Chest X-ray, arterial BLOOD gases, pulmonary function tests, and chest computed tomography (chest CT) are among the diagnostic procedures that may help identify the extent of pulmonary involvement and its effect on oxygenation.

Treatment is often CORTICOSTEROID MEDICATIONS to relieve inflammation, which may allow the lungs to return to normal function. The doctor may also prescribe ANTIBIOTIC MEDICATIONS to treat

secondary INFECTION if present, or when the cause of the pneumonitis is bacterial infection. Elimination of irritants, when known, prevents the pneumonitis from recurring. Most people recover fully and without complications after the inflammation subsides. Chronic pneumonitis may result in scarring (fibrosis) and permanent damage to pulmonary structures, however.

See also ASTHMA; HYPOXIA; MULTIPLE CHEMICAL SENSITIVITY SYNDROME; PLEURISY; PNEUMOCONIOSIS; PNEUMONIA.

pneumothorax A circumstance in which air gets in the pleural space (membrane space between the pleural linings of the lung and the thoracic cavity). Pneumothorax results in collapse of a portion of, or the entire, lung. Doctors identify different kinds of pneumothorax. They include

- spontaneous pneumothorax, in which the pneumothorax occurs for no identifiable reason or as a consequence of severe lung disease such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) or TUBERCULOSIS
- simple pneumothorax, in which air enters the pleural space and part of all of the lung collapses but there is no pressure on surrounding structures
- tension pneumothorax, in which the pneumothorax occurs and pressure continues to build in the pleural space, putting pressure on the heart and causing potentially life-threatening cardiovascular collapse
- traumatic pneumothorax, in which air enters the pleural cavity as a result of injury or surgery

Symptoms include DYSPNEA (shortness of breath) and sudden, sharp PAIN that worsens with deep BREATHING or coughing. Some people develop CYANOSIS (bluish hue to the lips and SKIN) that indicates the body is not receiving enough oxygen. TACHYCARDIA (rapid HEART RATE), TACHYPNEA (rapid breathing), and HYPOTENSION (low BLOOD PRESSURE) are also common. The diagnostic path includes AUSCULTATION, which often reveals reduced or absent BREATH SOUNDS, and chest X-RAY, which shows the area of lung collapse.

A pneumothorax that involves only a small portion of the lung often heals itself. A larger pneumothorax requires insertion of a chest tube (done with local ANESTHESIA) to remove the air and allow the lung to reinflate. Most people who require such treatment stay in the hospital until the affected lung returns to normal function and the doctor can safely remove the chest tube. About half of people who have one episode of spontaneous pneumothorax have a subsequent episode, though most people do not experience any permanent lung damage. People who are tall and thin are most vulnerable to spontaneous pneumothorax. Spontaneous pneumothorax is also more common among people who smoke.

See also BRONCHIECTASIS.

positive airway pressure Methods to maintain higher than normal air pressure against the inner walls of the bronchi and TRACHEA during BREATHING. Positive airway pressure may be a treatment for ATELECTASIS (collapsed lung), chronic RESPIRATORY FAILURE, and SLEEP APNEA. Positive airway pressure is also an important aspect of MECHANICAL VENTILATION.

The most common method of positive airway pressure is continuous positive airway pressure (CPAP), in which a small pump pushes a steady flow of air through a face mask to maintain enough pressure against the airways to keep them open and unobstructed during sleep. CPAP is a common and an effective treatment for sleep apnea. Bilevel positive airway pressure, or BiPAP, is a flexible variation of CPAP. The conventional CPAP device maintains a constant airway pressure for inhalation and exhalation. BiPAP provides additional pressure or support during inspiration to aid inhalation.

See also BRONCHUS; OXYGEN THERAPY; SLEEP APNEA.

postural drainage See CHEST PERCUSSION AND POSTURAL DRAINAGE.

pulmonary edema Abnormal fluid accumulation within the alveoli and the interstitial tissues of the LUNGS, typically resulting from CARDIOVASCULAR DISEASE (CVD) such as HEART FAILURE or CARDIOMYOPATHY. PNEUMONIA, ACUTE RESPIRATORY DISTRESS SYNDROME

(ARDS), smoke inhalation, near drowning, and high altitude can also cause pulmonary edema.

Pulmonary edema can be a life-threatening condition and requires immediate medical evaluation and treatment.

The accumulated fluid of pulmonary edema limits air from entering the alveoli, affecting the OXYGEN–CARBON DIOXIDE EXCHANGE. The consequence is inadequate oxygen diffusion into the BLOOD with resulting HYPOXIA.

Symptoms and Diagnostic Path

The symptoms of pulmonary edema tend to come on quickly and include

- DYSPNEA (difficulty BREATHING), often severe or worse when lying down
- frothy HEMOPTYSIS (coughing up bloody SPUTUM)
- diaphoresis (profuse sweating or chills with sweating)
- HEADACHE or light-headedness
- COUGH
- Wheezing or gurgling sounds when breathing

Respiratory failure can rapidly develop. The diagnostic path includes AUSCULTATION with a stethoscope to listen to BREATH SOUNDS, which typically reveals rales (crackles). A chest X-RAY shows the accumulated fluid. Arterial blood gases assess the extent of hypoxia. Diagnostic procedures to evaluate cardiovascular function include ELECTROCARDIOGRAM (ECG), ECHOCARDIOGRAM, and CARDIAC CATHETERIZATION if the doctor suspects CORONARY ARTERY DISEASE (CAD) or MYOCARDIAL INFARCTION.

Treatment Options and Outlook

Treatment begins with OXYGEN THERAPY to improve oxygenation and, if the edema is from heart failure, usually diuretic medications to help pull the excessive fluid into the circulation so the KIDNEYS can pass it from the body. Additional treatment targets the underlying cause of the pulmonary edema, which may be cardiovascular or pulmonary. High altitude pulmonary edema (HAPE) requires prompt oxygen therapy with descent to a lower altitude as soon as is feasible. Climbers sometimes underestimate the seriousness of HAPE until symptoms become overwhelming and life-threatening. Any climber, regardless of high-altitude acclimation and climbing experience, is vulnerable to HAPE and all climbers should be familiar with early symptoms.

Pulmonary edema is a serious circumstance that can result in death when not promptly recognized and treated. The underlying cause determines the outcome. When the cause is cardiovascular, treatment may include CORONARY ARTERY BYPASS GRAFT (CABG) or ANGIOPLASTY to improve the flow of blood to the HEART. Medications may strengthen the heart and stabilize HEART RATE in heart failure, improving the heart's ability to pump blood. With appropriate treatment, many people recover completely from pulmonary edema. When the cause is noncardiogenic, such as due to severe infection or ARDS, treatment targets reversing the underlying disease and providing respiratory support until lung function returns to normal.

Risk Factors and Preventive Measures

The primary risk factor for cardiogenic pulmonary edema is cardiovascular disease. The most effective preventive measures are those that reduce the risks for cardiovascular disease: No smoking, maintain appropriate weight, exercise daily, and eat nutritiously. It is also important to take medications for diagnosed conditions such as HYPERTENSION (high BLOOD PRESSURE) as prescribed.

See also ASCITES; ESOPHAGEAL VARICES; PULMONARY HYPERTENSION.

pulmonary embolism A BLOOD clot that blocks the flow of blood through the main pulmonary ARTERY, the right or left pulmonary artery, or branching arteries within the lobes and segments of the LUNGS. Untreated pulmonary embolism can cause respiratory distress or death; about 30,000 people die each year in the United States as a result of pulmonary embolism.

Pulmonary embolism is a life-threatening condition that requires emergency medical care.

Pulmonary embolism is a potential complication of blood clots that develop within the veins,

typically the deep veins of the legs. It most commonly develops as a consequence of venous stasis, in which the blood moves sluggishly through the veins. The blood's slow movement allows blood to pool, permitting clots to begin to form especially on and around the valves in the veins. Clot fragments or the entire clot can break free, floating through the bloodstream.

Because the veins become larger as they approach the HEART, the bloodstream easily carries the clots through the right heart and into the pulmonary arteries and the lungs. Occasionally the clot that causes a pulmonary embolism originates in the heart's right atrium. Large clots can occlude (block) the pulmonary arteries at the point where the right and left pulmonary arteries diverge (bifurcation of the pulmonary artery).

As a consequence of the intimate correlation between alveolar function and the flow of blood through the capillary network that enmeshes the alveoli, the loss of capillary flow resulting from pulmonary embolism effectively shuts down all alveoli beyond (distal to) the site of the occlusion. Any loss of functioning alveoli subsequently limits the ability of the lungs to convey oxygen to the blood. The larger the occluded artery, the more immediate and significant the pulmonary consequences.

Symptoms and Diagnostic Path

The symptoms of pulmonary embolism vary widely and can be subtle or may be as severe and immediate as those of HEART ATTACK, and are similar. Such symptoms include

- sudden, severe CHEST PAIN
- DYSPNEA (difficulty BREATHING)
- diaphoresis (breaking into a cold sweat)
- HYPOTENSION (low BLOOD PRESSURE)
- TACHYCARDIA (rapid heart rate)
- TACHYPNEA (rapid BREATHING)

A person who experiences a massive pulmonary embolism may have little time between feeling fine and going into shock and cardiovascular collapse. Smaller emboli or recurrent (chronic) pulmonary embolism episodes generally produce milder variations of these same symptoms along with productive COUGH and HEMOPTYSIS (blood in the SPUTUM).

The diagnostic path seeks immediately to determine whether the symptoms are cardiovascular (heart attack) or pulmonary. An ELECTROCARDIOGRAM (ECG) does not show evidence of acute cardiac injury in pulmonary embolism, which is the first major point of differentiation. Arterial blood gases show how severely the pulmonary embolism is affecting the body's oxygenation. Diagnostic imaging procedures the pulmonologist may conduct include COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), pulmonary angiography, and a specialized imaging procedure called ventilation/perfusion scan.

Treatment Options and Outlook

Hospitalization with intensive pulmonary support and immediate ANTICOAGULATION THERAPY is necessary for most circumstances of pulmonary embolism. The risk of death is highest within the first few hours of the embolism. Anticoagulation therapy targets preventing the formation of additional emboli. THROMBOLYTIC THERAPY ("clot buster" drugs) to dissolve the clots that have already formed is appropriate for some people. Surgery (either OPEN SURGERY or via catheterization) to mechanically break up the clot may be an option in severe situations. Recovery depends on the extent of lung affected, the existence of any underlying causes or health conditions, and the rapidity of diagnosis and treatment. People who recover from pulmonary embolism often require ongoing anticoagulation therapy though do not have significant permanent lung damage.

Risk Factors and Preventive Measures

Pulmonary embolism is most likely to occur in people who have restricted venous flow due to lower extremity VARICOSE VEINS or incompetent veins (veins that have lost elasticity and valve function), who are physically inactive, or who have recently had surgery or a major trauma (which means the body is forming clots for HEALING and also usually means limited physical movement). People who have untreated ATRIAL FIBRILLATION have increased risk for pulmonary embolism. OBESITY also increases the risk for pulmonary embolism because it exerts additional

resistance against the blood flowing through the veins. People who have an increased tendency to form clots (hypercoagulation) are also at increased risk of developing a clot or pulmonary embolism. Research suggests that as many as 80 percent of people who have DEEP VEIN THROMBOSIS (DVT) experience frequent pulmonary emboli. About half of the people who have one pulmonary embolism experience subsequent episodes.

Prevention often incorporates ongoing ANTICOAGULATION THERAPY in people at risk for pulmonary embolism, including those who have had a previous episode. Support stockings help the leg muscles to work more efficiently in massaging blood through the veins. For someone who has never had a pulmonary embolism, regular physical activity and maintaining healthy body weight help to lower the risk for clot formation. Frequent stretching of the legs, and getting up to walk for a few minutes every hour, can maintain effective circulation and venous return when taking long air flights or train or automobile trips to lower the risk for both DVT and pulmonary embolism. Postoperative recovery and recuperation regimens incorporate early ambulation (walking within hours of surgery) as well as progressive ambulation (walking for longer times and distances as recovery continues). When the person cannot ambulate, preventive measures may include compression stockings and anticoagulant medications.

See also COAGULATION; MYOCARDIAL INFARCTION; PLATELET AGGREGATION; POSTOPERATIVE CARE; STROKE; SURGERY BENEFIT AND RISK ASSESSMENT; WEIGHT LOSS AND WEIGHT MANAGEMENT.

pulmonary fibrosis A condition in which SCAR tissue replaces normal tissue in the alveoli, reducing the ability of the LUNGS to oxygenate the BLOOD. Many conditions of the lungs result in fibrosis, notably CYSTIC FIBROSIS and occupational PNEUMOCONIOSIS. Pulmonary fibrosis may also be idiopathic—that is, develop without an identifiable cause. Once the process of fibrosis begins in the lungs, it tends to be progressive. In many people the progression takes place over decades, resulting in slow decline of pulmonary function. Clubbing of the fingers is a characteristic indication of chronic HYPOXIA (insufficient oxygen reaching the tissues) such as results from pulmonary fibrosis.

Symptoms of pulmonary fibrosis include

- persistent dry COUGH
- DYSPNEA (shortness of breath) that worsens with exertion
- diminishing capacity for physical activity
- fatigue
- chest tightness, discomfort, or PAIN

The diagnostic path includes chest X-RAY, pulmonary function tests, and arterial blood gases. The pulmonologist may conduct additional imaging procedures, such as COMPUTED TOMOGRAPHY (CT) SCAN, to further assess structural changes in the lungs. BRONCHOSCOPY and lung biopsy may be necessary to rule out CANCER or to identify pathologic changes that characterize specific diseases.

Treatment depends on the underlying cause, if the diagnostic path can identify one. Generalized treatment may include CORTICOSTEROID MEDICATIONS to reduce INFLAMMATION, bronchodilator medications to relax and open the airways, and cough suppressants to relieve nonproductive coughing. These methods control symptoms and improve BREATHING in many people who have pulmonary fibrosis, especially in the early and middle stages of the condition. However, progressive pulmonary fibrosis typically results in RESPIRATORY FAILURE for which LUNG TRANSPLANTATION may be the only viable treatment option.

See also BRONCHIECTASIS; CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD); CYSTIC FIBROSIS AND THE LUNGS; INTERSTITIAL LUNG DISORDERS; NAILS.

R

rales See BREATH SOUNDS.

respiration rate The number of respiratory cycles a person completes in one minute. A typical healthy adult has a respiration rate of 15 to 20 per minute, measured by counting each inhalation or each exhalation (a respiratory cycle is one of each). Respiration rate normally is lower at rest and during sleep, and accelerates as well as intensifies with physical activity and exercise. Children have higher respiration rates than adults. The respiration rate typically increases with health circumstances such as INFECTION, FEVER, trauma, PAIN, and strong emotions such as fear. The brainstem regulates the respiration rate, in intimate coordination with other vital functions such as HEART RATE and BLOOD PRESSURE. The respiration rate remains at roughly a ratio of 1 to 4 with the heart rate (one breath for every four contractions of the HEART).

See also BREATHING; CARDIAC CYCLE.

respiratory cycle One repetition of the pattern of inhalation (BREATHING air into the LUNGS), OXYGEN–CARBON DIOXIDE EXCHANGE, and exhalation (breathing air out of the lungs). In health a typical adult completes 15 to 20 respiratory cycles a minute, called the RESPIRATION RATE. The brainstem regulates the respiratory cycle in response to feedback mechanisms from other body systems that indicate oxygen needs and consumption.

See also AEROBIC FITNESS; BREATHING EXERCISES; DYSPNEA; HYPERVENTILATION; TACHYPNEA.

respiratory failure The inability of the LUNGS to diffuse enough oxygen into the bloodstream to meet the body's needs. Respiratory failure may arise from end-stage pulmonary disease, extensive trauma, severe CARDIOVASCULAR DISEASE (CVD) or crisis (such as HEART ATTACK), neurologic damage or injury (such as SPINAL CORD INJURY, TRAUMATIC BRAIN INJURY [TBI], STROKE, or neurodegenerative disorder), or severe INFECTION (sepsis). Respiratory failure may be acute or chronic.

Acute respiratory failure is a life-threatening condition that results from the inability to breathe enough or the inability of the lungs to diffuse adequate amounts of oxygen into the blood, or a combination of both. Symptoms of acute respiratory failure typically are pronounced and include

- extreme DYSPNEA (shortness of breath or difficult BREATHING)
- CYANOSIS (bluish hue to the lips and SKIN)
- HYPOTENSION (low BLOOD PRESSURE)
- cardiovascular SHOCK

Treatment of acute respiratory failure requires oxygen administration and immediate resuscitative breathing or MECHANICAL VENTILATION; without prompt restoration of oxygenation, death is inevitable.

Chronic respiratory failure may also be life-threatening, though commonly the person accommodates the inadequate oxygenation through restricted physical activity and treatments such as OXYGEN THERAPY. Chronic respiratory failure is a consequence of progressive pulmonary disorders such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). Symptoms of chronic respiratory failure may be activity related and often include

- persistent COUGH
- dyspnea, especially with exertion
- diminished cognitive ability or confusion

- cyanosis
- fatigue
- edema (swelling, typically in the hands and feet)

Doctors measure and assess chronic respiratory failure through blood levels of oxygen (which are low) and carbon dioxide (which are high). People who have chronic respiratory failure also commonly have PULMONARY HYPERTENSION. Treatment for chronic respiratory failure attempts to improve oxygenation through OXYGEN THERAPY and medications such as bronchodilators and some situations corticosteroids. The underlying disease and the person's response to therapy are key factors in determining the overall treatment approach. When chronic respiratory failure results from end-stage pulmonary disease, treatment options are limited. Some people are candidates for LUNG TRANSPLANTATION.

See also APNEA; ATELECTASIS; BREATH SOUNDS; BRONCHIECTASIS; OXYGEN–CARBON DIOXIDE EXCHANGE; SUDDEN CARDIAC DEATH.

S

silicosis An obstructive condition of the LUNGS that develops with repeated and usually long-term exposure to crystalline silica (silica dust). Silicosis is a disease of occupational exposure. The silica dust causes irritation and INFLAMMATION of the airways and lung tissue. SCAR tissue forms when the inflammation heals, resulting in fibrosis that gradually overtakes healthy lung tissue. The fibrosis continues extending through the lungs even after exposure ends.

Health experts identify three forms of silicosis:

- chronic silicosis, the most common form, results from long-term exposure (10 to 20 years or longer) and generally is present as a disease entity in the lungs for 5 to 10 years before symptoms lead to its diagnosis
- accelerated silicosis, which shows rapidly progressive symptoms after 5 to 10 years of exposure
- acute silicosis, which occurs with exposure to high concentrations of silica dust and shows symptoms within weeks to months of exposure

A secondary complication, progressive massive fibrosis, may occur with accelerated or chronic silicosis. In progressive massive fibrosis the scarring is severe and results in extensive destruction of lung tissue and loss of lung function.

The US Occupational Safety and Health Administration (OSHA) began regulating silica exposure in the 1990s and currently monitors silica levels as well as cases of silicosis. Employees who work in occupations with silica exposure should wear appropriate protective equipment including filtered respirators to limit as much as possible the amount of silica dust they breathe. About 200 people die each year in the United States as a consequence of silicosis.

Symptoms and Diagnostic Path

The primary symptoms of silicosis are chronic COUGH and DYSPNEA (shortness of breath) that worsens with exertion. People who have acute silicosis may also have FEVER and experience rapid, unintended weight loss. The diagnostic path includes chest X-RAY, imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN, and pulmonary function tests. Characteristic findings with these diagnostic procedures in combination with a history of silica exposure allow the doctor to make a conclusive diagnosis.

People who have silicosis have high risk for developing TUBERCULOSIS, and many have latent (asymptomatic) tuberculosis when tested at the time of the silicosis diagnosis. Health experts recommend routine testing for tuberculosis as part of the diagnostic process for silicosis.

Treatment Options and Outlook

Treatment can only help manage symptoms such as cough. There are no specific treatments for the silicosis, and there is no known method of intervention to prevent the condition's progression. It is crucial to end the silica exposure to end further damage to the lungs, and for those who smoke cigarettes to stop. Treatment may also be necessary for tuberculosis in people who test positive, even if there are no symptoms of the INFECTION. The course of progression often extends over decades, though does result in persistent decline of pulmonary function. Prevention remains the most effective therapeutic approach.

Risk Factors and Preventive Measures

Occupational exposure is the risk factor for silicosis. Appropriate personal protective equipment in combination with work-site dust management methods has the potential to prevent nearly all cases of silicosis. New cases of silicosis have steadily declined in the United States since the implementation of OSHA regulations limiting exposure, a trend health experts expect to continue. Researchers believe the silica dust interferes with the IMMUNE SYSTEM's ability to protect against certain kinds of infection, notably tuberculosis. Health experts recommend annual tuberculosis testing for everyone diagnosed with silicosis.

OCCUPATIONS AT RISK FOR SILICOSIS

abrasive blasting	agricultural plowing
ceramics	foundry core room
foundry shakeout	glass etching
glass manufacturing	jack hammering
masonry work	mineral mining
pottery	quarry work
road construction	rock blasting
rock drilling	rock tunneling
sandblasting	soap and detergent manufacturing
stone chipping and crushing	stone grinding
stone cutting	

See also ANTHRACOSIS; ASBESTOSIS; BERYLLIOSIS; BYSSINOSIS; PNEUMOCONIOSIS.

smoking and pulmonary disease Cigarette smoking is the leading cause of health conditions affecting the LUNGS and accounts for 90 percent of LUNG CANCER in the United States. Cigarette smoking is also the leading cause of many forms of CARDIOVASCULAR DISEASE (CVD), including HYPERTENSION, ATHEROSCLEROSIS, ISCHEMIC HEART DISEASE (IHD), CORONARY ARTERY DISEASE (CAD), and PERIPHERAL VASCULAR DISEASE (PVD). Though the correlation between cigarette smoking and lung cancer has been known since the 1940s and widely publicized since the 1964 landmark report *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service*, nearly 49 million Americans currently smoke. About one in six has at least one significant health condition that is a direct consequence of smoking. The longer a person smokes, the higher the risk for developing a smoking-related health condition.

Smoking and Pulmonary Function

The first few puffs of every cigarette paralyze the cilia, the hairlike structures that line the airways and sweep mucus from the lungs. NICOTINE from the smoke immediately passes across the alveolar membrane into the BLOOD, entering the circulation within seconds. A potent central NERVOUS SYSTEM STIMULANT and vasoconstrictor, nicotine causes smooth MUSCLE fibers to contract, contributing to cerebrovascular and cardiovascular disease such as STROKE and HEART ATTACK. Nicotine remains active in the circulation for about 20 minutes after the last puff from the cigarette, keeping the airways constricted.

One of the most hazardous chemicals in cigarette smoke is carbon monoxide, which binds more strongly with HEMOGLOBIN than oxygen. Hemoglobin molecules will not release carbon monoxide to bind with oxygen, thus carbon monoxide blocks oxygen diffusion into the blood. Carbon monoxide levels in the blood can reach 5 to 7 percent with smoking a single cigarette, dropping OXYGEN SATURATION to near 90 percent. The other byproducts of combustion from cigarette smoke can result in direct toxicity to the lungs.

Smoking and Obstructive Lung Diseases

Tar and smoke particulates that enter the airways and lungs with each cigarette cause irritation and INFLAMMATION. Over time SCAR tissue replaces lung tissue as the body attempts to repair itself from repeated damage and protect itself from further damage. This scar tissue gradually destroys the alveoli and bronchioles, the lung's smallest structures, and eventually becomes pervasive within the lungs. The consequence is CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), which accounts for more than 70 percent of pulmonary disease related to smoking. COPD is the leading reason for LUNG TRANSPLANTATION in the United States and is also the leading form of noncancer lung disease. Once the damage of COPD occurs, it is permanent.

Lung Cancer

Cigarette smoke contains about 4,000 identifiable chemicals, more than 60 of which are identified carcinogens (cancer-causing substances). Among them are tar, arsenic, polycyclic aromatic hydrocarbon (PAH) compounds, formaldehyde, and nitrosamines. Smoking accounts for more than 90 percent of LUNG CANCER in the United States. Among cancers, lung cancer is the leading killer of both men and women. Part of the reason the outlook is so poor for lung cancer is that by the time it shows symptoms it is fairly advanced and often has spread to other organs throughout the body.

Pulmonary Benefits of Smoking Cessation

Much, though not all, of the damage cigarette smoking does will gradually repair itself when the person no longer smokes. The rate of decline of lung function will slow, and chronic cough and sputum production often improve. Cardiovascular risk also drops significantly after smoking cessation. Risk for head and neck and lung cancers also decreases.

See also ANTISMOKING EFFORTS; ASBESTOSIS; ASTHMA; ENVIRONMENTAL CIGARETTE SMOKE; SMOKING AND HEALTH.

sputum The mucus and secretions the pulmonary tract produces, mixed with debris and foreign matter that enter the airways. Sputum is a normal body fluid, though excessive amounts of sputum often signal pulmonary disease. The color and consistency of sputum provide clues about the health of the LUNGS and airways, though are not reliable diagnostic characteristics by themselves. Sputum culture is the only way to know whether an INFECTION is bacterial. A reliable sputum culture requires deep coughing to bring sputum from within the lungs.

See also HEMOPTYSIS.

stridor See BREATH SOUNDS.

suffocation See ASPHYXIATION.

T–W

tachypnea An abnormally rapid RESPIRATION RATE. BREATHING is also usually shallow. The normal respiration rate for healthy adults is 15 to 20 respiratory cycles per minute. In tachypnea the respiration rate can be two to four times normal. Breathing may appear labored, and when the body is not able to meet its needs the person may look cyanotic (pale or bluish) if the tissues are receiving inadequate oxygen. Tachypnea is a symptom of numerous health conditions ranging from FEVER to serious INFECTION such as PNEUMONIA. In transient tachypnea of the newborn, an infant develops a pattern of tachypneic breathing that lasts 24 to 72 hours after birth. Doctors believe this form of tachypnea, which resolves without treatment or complications, occurs as a mechanism for the infant to clear residual AMNIOTIC FLUID from the LUNGS.

See also CYANOSIS; DYSPNEA; HYPERVENTILATION.

thoracentesis The removal of fluid from the pleural cavity (the space between the pleural surfaces of the lung and thoracic cavity). The doctor typically uses chest X-RAY, ULTRASOUND, or COMPUTED TOMOGRAPHY (CT) SCAN to assess the appropriate site for the thoracentesis and may use any of these imaging procedures to guide the process of the thoracentesis. After anesthetizing (numbing) the SKIN and tissues at the site, the doctor inserts a large-gauge needle between the ribs and into the pleural cavity to withdraw pleural fluid.

Thoracentesis may be diagnostic, in which case the doctor withdraws a small amount of fluid for laboratory examination of the cells and any pathogens it contains. The doctor may conduct diagnostic thoracentesis to evaluate circumstances such as

- CHEST PAIN and other symptoms that suggest PLEURISY or PLEURAL EFFUSION
- mesothelioma, a CANCER related to ASBESTOSIS or asbestos exposure
- identification of infection (bacterial or tuberculosis)
- staging of LUNG CANCER

Thoracentesis may also be therapeutic, such as to drain a major pleural effusion. Potential complications of thoracentesis include vasovagal NERVE stimulation that causes SYNCOPE (fainting) bleeding, INFECTION, bleeding, and PNEUMOTHORAX. Most procedures are uncomplicated and discomfort is usually mild and temporary.

See also ATELECTASIS; STAGING AND GRADING OF CANCER; THORACOTOMY.

thoracotomy A major OPERATION in which the surgeon opens the chest cavity to remove part or all of a lung. Surgeons most commonly perform thoracotomy to treat LUNG CANCER or severe trauma to the lungs. Other reasons for thoracotomy include LUNG ABSCESS that does not respond to antibiotic therapy, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) in which there is significant alveolar destruction and lung volume resection may be of benefit, severe BRONCHIECTASIS with bleeding requiring resection of part of the lung, biopsy of lung tissue or suspected tumor, and LUNG TRANSPLANTATION. There are three kinds of thoracotomy:

- wedge resection removes a small segment of lung tissue
- lobectomy removes an entire lobe of the lung
- pneumonectomy removes a whole lung

In lung transplantation, the surgeon first performs pneumonectomy and then transplants the donor replacement lung. Thoracotomy entails a hospital stay of up to 10 days, depending on the kind of surgery, and a recuperation period of two to four months though some people can return to most of their normal activities within six to eight weeks. Additional treatment, such as RADIATION THERAPY or CHEMOTHERAPY for lung cancer, may extend the recuperation period.

Surgical Procedure

The doctor performs thoracotomy with the person under general ANESTHESIA. The placement and length of the incision depends on the kind of thoracotomy and the reason for performing it. The incision must be between the ribs, and the surgeon must either spread the ribs (using an instrument called a rib spreader) or remove a portion of rib to gain access to the thoracic cavity. The surgeon removes the intended segment, lobe, or entire lung, and places tubes that will drain air, BLOOD, and other fluids during HEALING. The operation may take two to six hours, longer for lung transplantation. The person then remains in the recovery room until the anesthesia wears off, with intensive nursing care to maintain BREATHING and other vital functions. Less invasive approaches that use fiberoptic scopes and a smaller incision are now an option, particularly for biopsies. Such MINIMALLY INVASIVE PROCEDURES allow quicker operative times and recuperation.

Risks and Complications

Because thoracotomy breaches the thoracic cavity, there are significant risks involved with this operation. The most common are bleeding, infection, and PNEUMOTHORAX. These risks are potentially life-threatening though are usually readily treatable and survivable. Complications include RESPIRATORY FAILURE and RECURRENCE of the circumstance that made the operation necessary. Removal of a complete lung results in the remaining structures of the thoracic cavity shifting position, which can alter HEART function, gastric (STOMACH) function, and breathing.

Outlook and Lifestyle Modifications

Many people spend the first 48 to 72 hours following surgery in the intensive care unit (ICU). MECHANICAL VENTILATION ensures that the remaining lung structure inflates fully to provide adequate oxygenation. As the healing process progresses the affected lung (after lobar resection), or remaining lung when the operation is pneumonectomy, expands to fill the thoracic cavity and pulmonary function improves. Most people can sustain strong pulmonary function with only one lung when the remaining lung is healthy and overall health is good. Lifestyle modifications and prognosis (outlook) vary with the underlying health condition.

See also SMOKING CESSATION; SURGERY BENEFIT AND RISK ASSESSMENT.

trachea The major airway leading from the THROAT to the LUNGS. The trachea extends about four and a half inches from the top of the throat to the center of the chest. The sternum (breastbone) in the front and the spine in the back protect the trachea for much of its length. The front of the trachea arches more than the back of the trachea, producing an oval rather than round tubular structure with a diameter (from side to side) of about an inch. The trachea terminates in two branches, the right main BRONCHUS that goes to the right lung and the left main bronchus that goes to the left lung.

The trachea is made of smooth MUSCLE tissue along the back wall with 16 to 20 C-shaped bands of CARTILAGE running along its length. The cartilage rings give the trachea stability and resistance against the pressure of air flow into and out of the lungs. Thousands of hairlike structures called cilia line the inner layer of the trachea, the tracheal epithelium. The cilia move in wavelike patterns to push secretions and foreign matter, such as dust and particles, out of the airways. The epithelial cells secrete mucus, which keeps the inner trachea moist. The mucus helps humidify the air as it flows into the lungs, and lubricates the air's passage. The mucus also traps foreign material so the cilia can sweep it from the airways. Coughing expels air rapidly and forcefully from the lungs, pushing SPUTUM (pulmonary mucus and the debris it contains) into the throat for removal from the body.

For further discussion of the trachea within the context of pulmonary structure and function

please see the overview section "The Pulmonary System."

See also ALVEOLUS; EPIGLOTTIS; TRACHEOSTOMY.

tracheostomy A surgical opening created in the TRACHEA to allow air to enter the LUNGS, bypassing the upper THROAT and MOUTH. A tracheostomy may be temporary or permanent. The doctor may perform a tracheostomy when extensive surgery such as to treat laryngeal CANCER results in removing the shared structures of the throat that allow air to flow into the trachea, or when neurologic damage necessitates long-term MECHANICAL VENTILATION. SWALLOWING DISORDERS that impede normal epiglottal function (which keeps food and water from entering the trachea) and SLEEP APNEA that fails to respond to other treatments may also make tracheostomy necessary.

In most cases the doctor performs tracheostomy with the person under general ANESTHESIA. The incision is typically between the second and third or third and fourth tracheal cartilages in the front of the neck, to make an opening about an inch to an inch and a quarter (2 to 3 centimeters) in length. The doctor then inserts a tube into the opening to maintain a passageway into the trachea. The kind of tube and finishing process for the incision depends on whether the doctor intends the tracheostomy to be temporary or permanent. An inflatable cuff may hold the tracheostomy tube in place, though some designs are cuffless. Most tracheostomies use an inner and outer cannula (tube), allowing removal of the inner cannula for cleaning. A device called an obturator allows changing of the entire tracheostomy tube and guides reinsertion of the new tube.

Most people who are conscious are able to resume regular eating and speaking. Speech requires closing off the tracheostomy tube to bring air through the throat and past the VOCAL CORDS. Potential complications of tracheostomy include bleeding after the OPERATION, INFECTION, and blockage of the tube with mucus or foreign material that enters the tube from the outside. Conscientious hygiene, including daily cleansing of the tracheostomy site and tube, is essential. It is important to humidify the air breathed into the tracheostomy, such as with a room humidifier or moist gauze (rewetted as needed) placed over the tube opening. Home health nursing agencies provide education and training in how to care for a tracheostomy for people who have tracheostomies and their family members or caregivers. Even a long-term stoma will heal closed should the person's condition improve such that normal BREATHING ability returns and the doctor can remove the tube.

See also EPIGLOTTIS; OXYGEN THERAPY; SPINAL CORD INJURY; TRAUMATIC BRAIN INJURY (TBI).

wheeze See BREATH SOUNDS.

THE IMMUNE SYSTEM AND ALLERGIES

The IMMUNE SYSTEM protects the body from INFECTION. Allergies represent an inappropriate response from the immune system toward harmless substances. Doctors (MDs and DOs) who treat conditions of the immune system may be internists or immunologists. Doctors who specialize in treating allergies are allergists, and those who specialize in treating RHEUMATOID ARTHRITIS and related AUTOIMMUNE DISORDERS are rheumatologists.

Structures of the Immune System

LYMPH
lymph nodes
B-CELL LYMPHOCYTE
  plasma cell
  memory B-cell
T-CELL LYMPHOCYTE
  cytotoxic (killer) T-cell
  memory T-cell
  helper T-cell
  suppressor t-cell
NATURAL KILLER (NK) CELL
complement factors
MONOCYTE
MACROPHAGE
GRANULOCYTE
  basophil
  eosinophil
  neutrophil
MAST CELL
M cell
adenoids
tonsils
THYMUS
PEYER'S PATCHES
APPENDIX
MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT)
SKIN-ASSOCIATED LYMPHOID TISSUE (SALT)
NOSE-ASSOCIATED LYMPHOID TISSUE (NALT)
BRONCHIAL-ASSOCIATED LYMPHOID TISSUE (BALT)
GUT-ASSOCIATED LYMPHOID TISSUE (GALT)
VASCULAR-ASSOCIATED LYMPHOID TISSUE (VALT)

Functions of the Immune System

The immune system's role is to protect the body from infection. Infection, from the immune system's perspective, is any activity from foreign entities that causes damage to cells. It does so through a complex and intricate integration of organs, tissues, cells, and molecules.

Each day the BONE MARROW releases billions of monocytes and granulocytes, also called polymorphonuclear cells (PMNs), into the BLOOD circulation. Monocytes circulate in the blood for about 24 hours and then migrate into the LYMPH tissues, LIVER, and the various MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) structures throughout the body. Known as macrophages after their migration, these cells participate in ANTIGEN processing as well as continued PHAGOCYTOSIS (consumption of cellular debris). Granulocytes (neutrophils, basophils, and eosinophils) are instrumental in the body's inflammatory response, which is integral to HEALING in normal immune function as well as responsible for much of the distress of a HYPERSENSITIVITY REACTION—ALLERGY—when the immune system malfunctions.

The workhorse cells of the immune system are the lymphocytes, which from birth divide into two camps: B-cell lymphocytes, which patrol the blood and lymph on the alert for invaders, and T-cell lymphocytes, which respond to the call of B-cell lymphocytes when invaders penetrate the body's barriers. B-cell lymphocytes come to maturity in the bone marrow and regulate ANTIBODY-MEDIATED IMMUNITY. T-cell lymphocytes come to maturity in the THYMUS and regulate CELL-MEDIATED IMMUNITY. Lymphocytes circulate in the blood and the lymph, and also reside in lymph organs and tissues throughout the body. The SPLEEN contains about half the body's supply of lymphocytes.

Perhaps more than any other system of the body the immune system is one of molecular function. The entire function of the immune system centers on the ability of immune cells to distinguish cells that belong to the body—self cells—from cells that do not belong to the body—nonself cells. It does so through molecular mark-

ers called antigens. Lymphocytes, natural killer (NK) cells, macrophages, and the complement factors—a collection of substances that, when activated (the COMPLEMENT CASCADE), form potent chemical structures—key onto these antigens like lasers onto targets. Cells bearing self antigens continue unimpeded about their business in the body. Those bearing nonself antigens are tagged for destruction by another set of molecular markers, antibodies, that specialized B-cell lymphocytes called PLASMA cells produce. Each individual antigen generates a different ANTIBODY; millions of antibodies circulate in the blood and lymph.

Filling out the immune system's defense are specialized clusters of lymphoid tissue that line each point of access into the inner body: SKIN, NOSE, airways, gastrointestinal system, and even the blood vessels. These clusters—known collectively as the mucosa-associated lymphoid system—are like guard posts protecting the body's vulnerabilities. MALT contains abundant populations of lymphocytes, mast cells, and macrophages that detect and intercept millions of microbes, viruses, toxins, and irritants before they can breach the inner body.

Health and Disorders of the Immune System

In health the immune system is an amazing network of cells and molecules that patrol every pathway of the body. Most of the time, the immune system goes about protecting and ridding the body from invading pathogens without drawing any notice to its activities. Only when the immune system is too efficient—causing hypersensitivity reactions or autoimmune disorders—or ineffective—allowing infection or cancer—does its existence become unpleasantly apparent.

Inflammation: the front line The immune system's first response primary weapon is INFLAMMATION. Inflammation floods the affected tissues with infection-fighting molecules. Plasma, the liquid component of blood, carries these molecules and delivers them to the site of the infection. The familiar swelling of inflammation is the body's "caution: IMMUNE RESPONSE at work" sign. Inflammation causes PAIN, which encourages if not forces limited activity of the affected area. This allows plasma to thoroughly saturate the area, speeding healing and recovery. Inflammation may also cause FEVER, yet another inducement to take it easy. As unpleasant as these symptoms are, they serve notice that the immune system is on task.

Autoimmune disorders: attacking self cells Inflammation sometimes gets out of hand. The immune response may not recognize that its task is over. Inflammation may become so severe that it impedes the flow of blood, threatening the well-being of the body in other ways. ANTIBIOTIC MEDICATIONS may be necessary to bring in another flank of attack against the PATHOGEN. Or a malfunction of the immune system may erroneously mark self cells as invaders, directing the immune response to attack structures of the body that contain the cells. These are autoimmune disorders—such as RHEUMATOID ARTHRITIS, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and type 1 DIABETES.

Allergies: mistaken identity About 50 million Americans have allergies, mostly to pollens, molds, foods, animal dander, and medications. More than 18 million adults and 7 million children in the United States have seasonal allergies that cause ALLERGIC RHINITIS, ALLERGIC ASTHMA, and ALLERGIC CONJUNCTIVITIS—a triad of hypersensitivity reactions known collectively as hay fever. Another 9 million Americans, two thirds of them children, have FOOD ALLERGIES.

With allergies, the immune system turns not against the body itself but against harmless substances the body encounters, misidentifying them as dangerous intruders. Plasma cells then generate antibodies that perceive the molecular markers of these substances—allergens—as harmful and launch an immune response upon detecting their presence. Hypersensitivity reactions cause symptoms that range from annoying to life-threatening. It often is not possible to escape the reach of an ALLERGEN; treatment becomes the only recourse for relieving symptoms.

Immunodeficiency: AWOL Sometimes the immune system fails to function properly because key components are deficient or missing. Genetic errors may result in an absence of T-cell lymphocytes, B-cell lymphocytes, complement factors, immunoglobulins, or other substances necessary to integrate the immune response. Such deficits increase vulnerability to infection and, when severe, threaten life. The most significant acquired immunodeficiency is HIV/AIDS, which results from

infection with a VIRUS that hijacks and then destroys certain T-cell lymphocytes. There are treatments but as yet no cures for most immunodeficiencies, including HIV/AIDS.

Cancer: treacherous betrayal One of the greatest mysteries about immune function is cancer, the unregulated growth of cells. Ordinarily the immune response detects and destroys abnormal cells in the body, even when they are self cells. Cancer represents the ultimate betrayal of the immune system by self cells that dangerously mutate yet maintain enough self-antigens to escape detection. There comes a point in a cancer's development when tumor necrosis factors (TNFs), potent antitumor substances, are no longer able to squelch the errant growth. Some tumors seem able to avoid activating TNFs at all.

DISORDERS OF IMMUNE FUNCTION

ALLERGIC ASTHMA	ALLERGIC CONJUNCTIVITIS
ALLERGIC DERMATITIS	ALLERGIC RHINITIS
ANAPHYLAXIS	ANGIOEDEMA
ANKYLOSING SPONDYLITIS	ATOPY
autoimmune ADDISON'S DISEASE	autoimmune HEPATITIS
BULLOUS PEMPHIGOID	COMMON VARIABLE IMMUNODEFICIENCY (CVID)
dermatomyositis	DISCOID LUPUS ERYTHEMATOSUS (DLE)
DIABETES type 1	GRAFT VS. HOST DISEASE
FOOD ALLERGIES	Hashimoto's THYROIDITIS
GOODPASTURE'S SYNDROME	HYPERSENSITIVITY REACTION
GRAVES'S DISEASE	INFLAMMATORY BOWEL DISEASE (IBD)
HIV/AIDS	MULTIPLE MYELOMA
IgA NEPHROPATHY	MYASTHENIA GRAVIS
LEUKEMIA	PARTIAL COMBINED IMMUNODEFICIENCY (PCID)
lymphoma	POLYMYOSITIS
MULTIPLE SCLEROSIS	RHEUMATOID ARTHRITIS
organ transplant rejection	SCLERODERMA
PEMPHIGUS	SJÖGREN'S SYNDROME
pernicious ANEMIA	SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
REITER'S SYNDROME	
SARCOIDOSIS	
SEVERE COMBINED IMMUNODEFICIENCY (SCID)	
VASCULITIS	

Traditions in Medical History

Until the discovery of BACTERIA and viruses in the 19th century, doctors had little understanding for how the body contained and fought infection. Recognizing fever as a sign of healing led to efforts to "sweat out" the infection. Bloodletting was long a tradition for treating all kinds of ailments. The body's natural ability and tendency to overcome most infections gave credence to these and other methods. With the recognition of microbes and their role in pathogenesis (process of infection), research leapfrogged to greatly expanded understanding of immune system components and their functions.

Contemporary research has shown that some pre–MICROBE era therapeutic efforts have merit for bolstering immune function. Herbs such as ECHINACEA, GOLDENSEAL, and FEVERFEW boost immune response. Licorice root, turmeric, ginger, white willow (the forerunner of aspirin), witch hazel, and GREEN TEA are effective anti-inflammatory agents. Vitamins and minerals aid the intricate biochemical conversions essential for immune function. Antioxidants clear away molecular debris. Nature, as it turns out, staunchly supports the immune system.

Breakthrough Research and Treatment Advances

One of the most significant breakthroughs in disease management came with the introduction of vaccines in the mid-20th century. Before 1950, infection was the leading cause of death among Americans. The debut of antibiotic medications at the end of World War II was a tremendous stride in the ability to fight bacterial infections. But antibiotics are ineffective against viruses. In 1950 the viral infection POLIOMYELITIS was the leading cause of PARALYSIS among Americans; a decade later vaccination had made polio a rare condition. The World Health Organization (WHO) declared SMALLPOX, the first infection for which there was a successful VACCINE, eradicated in nearly all parts of the world in 1970—another landmark triumph in manipulation of the immune system to protect the body against infection without actually acquiring the infection. Today vaccines have made rare many diseases that were once common killers.

As researchers learn more about immune function and disease processes, the emphasis is shifting from treating the disease to preventing its development. Most CARDIOVASCULAR DISEASE (CVD), the leading cause of death among Americans, stems from a combination of lifestyle factors and inflammatory response. Though doctors have long

believed ATHEROSCLEROSIS (deposits of atherosclerotic plaque within the walls of the arteries) caused inflammation, recent research indicates the reverse is the case: inflammation attracts atherosclerotic deposits. Though further research is necessary to substantiate these findings, the result could be an entirely new perspective and approach for preventing cardiovascular disease.

Other research focuses on manipulating the immune system to "turn off" autoimmune disorders such as type 1 diabetes and rheumatoid arthritis, conditions that contribute to significant disability. Cancer research also is looking to the immune system to treat, cure, and prevent cancer. MONOCLONAL ANTIBODIES (MABS), genetically engineered molecules, can be laced with radioactive isotopes and targeted to the antigens on the cell surfaces of cancer cells, selectively killing them without damaging healthy cells. Researchers also believe it is possible to "teach" the immune system to recognize cancer cells and use its own resources to destroy them. Cancer vaccines are one direction of such research; molecular manipulation is another.

A

active immunity Long-term, acquired immune protection. Active immunity, also called acquired immunity, results from fighting an INFECTION or receiving a VACCINE that stimulates ANTIBODY response. In many circumstances active immunity is lifelong.

See also ANTIBODY-MEDIATED IMMUNITY; CELL-MEDIATED IMMUNITY; PASSIVE IMMUNITY.

aging, effects on immune response At birth the IMMUNE SYSTEM is fairly undeveloped. The infant relies largely on the carryover of maternal immune components for about the first six weeks of its life, while the infant's body builds its own immune system. By age four months, maternal IMMUNITY wears off and the infant's immune system is on its own (though an infant who is BREASTFEEDING continues to receive antibodies and limited immune support from his or her mother). Immunity reaches full STRENGTH in early childhood, a level at which it continues until about age 40.

After age 40, the effectiveness of the immune system begins to diminish. T-cell lymphocytes and macrophages respond more slowly. Levels of complement (protein factors essential for ANTIBODY–ANTIGEN binding) and of antibodies drop off. The immune system is slower to differentiate B-cell lymphocytes to antigen-producing PLASMA cells, and plasma cells produce lower quantities of antibodies. The immune response to disease as well as to vaccines becomes slower and less effective, increasing susceptibility to serious INFECTION (such as INFLUENZA and PNEUMONIA) from pathogens. The amounts and activity of MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) decrease in areas such as the LUNGS, further reducing the body's ability to reject infection from invading pathogens. Decades of exposure to antigens mean more lymphocytes are sensitized for specific antigens, leaving fewer to become sensitized to new antigens. The IMMUNE RESPONSE summons T-cell lymphocytes less quickly to the scene of an infection.

Changes in antigens and antigen recognition also occur, resulting in a decreased ability of the immune system to distinguish between self and nonself antigens. Cells may acquire a mix of antigens that makes them appear foreign, initiating an inappropriate immune response (autoimmune disorder) that damages an organ or structure. Or the immune system may fail to detect the change in antigens on the surfaces of cell membranes of cells that become cancerous, allowing cancer tumors to develop. AUTOIMMUNE DISORDERS and cancer consequently become more common with advancing age.

Measures to prevent infection can help offset age-related immune changes to some degree. Diligent HAND WASHING and avoiding exposure to other people who have COLDS or influenza may prevent the spread of these infections. ECHINACEA and GOLDENSEAL are herbal remedies that can boost immune function after an exposure to common pathogens. GAMMAGLOBULIN may boost the immune response in circumstances such as exposure to HEPATITIS. Older people often benefit from more aggressive antibiotic therapy—ANTIBIOTIC MEDICATIONS administered early in the infection process—to help them fight infections they do develop.

See also ANTIBODY-MEDIATED IMMUNITY; CELL-MEDIATED IMMUNITY; COMPLEMENT CASCADE; HEALING; IMMUNOSENESCENCE; LYMPHOCYTE; MACROPHAGE; T-CELL LYMPHOCYTE.

allergen A harmless substance, also called a hapten, that causes an exaggerated response from the

IMMUNE SYSTEM called a HYPERSENSITIVITY REACTION. For reasons researchers do not fully understand, the immune system produces antibodies for the substance that result in the IMMUNE RESPONSE perceiving the substance as a foreign invader. When the allergen contacts or enters the body, the antibodies attack it. Nearly any substance can be an allergen. DESENSITIZATION is a treatment for allergies that exposes the person to progressive doses of the allergen to increase the body's tolerance for the presence of the allergen and diminish the hypersensitivity reaction.

COMMON ALLERGENS

almonds	animal dander	aspirin (salicylates)
bee stings	cashews	cockroaches
dust and dust mites	eggs	fish
fragrances and perfumes	fungi	grasses
lanolin	latex	milk
molds	nickel	peanuts
pecans	penicillin	pollens
shellfish	smoke	strawberries
SOY	sulfa	wheat

See also ALLERGY; ALLERGY TESTING; ANAPHYLAXIS; ANTIBODY; ANTIGEN; ASTHMA; LIVING WITH ALLERGIES; MULTIPLE CHEMICAL SENSITIVITY SYNDROME.

allergic asthma A HYPERSENSITIVITY REACTION (allergic reaction) that involves the airways (bronchi). allergic ASTHMA is a type I or IMMUNOGLOBULIN E (IgE) reaction. Mast cells in the bronchial membranes release HISTAMINE, PROSTAGLANDINS, and LEUKOTRIENES. These substances cause itching and swelling of the bronchial membranes, resulting in wheezing and the sensation of chest tightness.

Cockroach droppings are the most frequent cause of allergic asthma. Other common allergens for allergic asthma include pollens (trees, grasses, and weeds), dust and dust mites, cigarette smoke, molds, and pet dander (especially cat dander). About 70 percent of people who have allergic asthma also have ALLERGIC RHINITIS, also called seasonal allergies or hay FEVER.

The diagnostic path focuses on separating allergic from nonallergic asthma. Though the symptoms are the same, the mechanisms and treatment approaches are different. Symptoms of allergic asthma include wheezing, shortness of breath (DYSPNEA), sensation of being unable to get enough air, and coughing. A severe hypersensitivity reaction, ANAPHYLAXIS, may occur if the bronchi swell enough to prevent the flow of air into the LUNGS.

ANAPHYLAXIS is a potentially life-threatening condition that requires immediate care from a doctor or hospital emergency department.

Treatment for allergic asthma may include oral and inhaled ANTIHISTAMINE MEDICATIONS, corticosteroid medications, and leukotriene receptor antagonist medications. Omalizumab (Xolair), a monoclonal antibody administered via subcutaneous injection, dramatically drops IgE levels in the BLOOD circulation, effectively stopping the hypersensitivity reaction before it causes symptoms. The most effective treatment is avoiding known or suspected allergens, though this is not always possible. ALLERGY TESTING can determine the specific allergens responsible for symptoms. DESENSITIZATION, in which the allergist exposes the person to small but increasing doses of the allergen over time, can help reduce the immune response to the allergen.

See also ALLERGIC CONJUNCTIVITIS; ALLERGIC DERMATITIS; ALLERGY; ANTIGEN; ATOPY; BREATH SOUNDS; CYTOKINES; LIVING WITH ALLERGIES; MONOCLONAL ANTIBODIES (MABS).

allergic conjunctivitis A type I (IMMUNOGLOBULIN E [IgE]) HYPERSENSITIVITY REACTION, commonly called an allergic reaction, that affects the membranes that line the inner eyelids (conjunctiva). Sometimes the irritation also reddens the white part of the eye (sclera). Allergic CONJUNCTIVITIS features red and swollen conjunctiva with excessive tearing and itching of the eyes and sometimes a white discharge. PHOTOPHOBIA (heightened sensitivity to light) is common. Because these symptoms also suggest viral or bacterial conjunctivitis (pink eye), which are infections, particularly when the discharge is yellow or green, a doctor should examine the eyes and assess the symptoms to make the correct diagnosis. Treatment differs according to the cause.

EYE irritation that interferes with vision, causes PAIN, or follows injury to the eye requires a doctor's prompt evaluation.

The most common form of allergic conjunctivitis develops seasonally when airborne pollens are high. Some people develop allergic conjunctivitis with exposure to allergens such as dust and pet dander (especially cat dander) as part of a broader ALLERGY picture. People who have seasonal allergies (ALLERGIC RHINITIS), ALLERGIC ASTHMA, or other ATOPY conditions may have a GENETIC PREDISPOSITION for type I hypersensitivity reactions that puts them at higher risk for developing allergic conjunctivitis as well.

Treatment for allergic conjunctivitis combines avoiding the responsible ALLERGEN with EYE drops that contain an antihistamine or, for severe symptoms, a corticosteroid (anti-inflammatory medication that suppresses the IMMUNE RESPONSE). ANTIHISTAMINE MEDICATIONS neutralize the histamine responsible for the allergic response. Systemic antihistamine medications (allergy relief products) may also help, especially when there are accompanying allergy symptoms such as allergic rhinitis. Natural tears eye drops can restore moisture to eyes that are scratchy and dry. Allergic conjunctivitis generally resolves when exposure to the allergen ends, which may be the end of allergy season when seasonal allergies (hay fever) are responsible.

See also ALLERGIC DERMATITIS; DRY EYE SYNDROME; INFECTION; LIVING WITH ALLERGIES.

allergic dermatitis A HYPERSENSITIVITY REACTION (allergic reaction) that affects the SKIN, usually in response to contact with an ALLERGEN. As with all hypersensitivity reactions, the first exposure to the allergen produces no symptoms. In reaction to the exposure, however, the IMMUNE SYSTEM produces antibodies for the allergen. Subsequent exposures to the allergen then do produce symptoms. Abundant immune cells reside in the epidermis, the inner layer of skin that contains living cells, to react to the allergen.

Most allergic dermatitis is a type IV, or delayed, hypersensitivity reaction. Symptoms generally affect only the area of contact and begin to emerge 24 to 36 hours after the contact, though may start within hours to a week later. Sometimes there can be repeated exposure before the hypersensitivity reaction occurs, though most commonly the second exposure triggers the ALLERGY.

A less common but more severe form of reaction is atopic dermatitis, a chronic type I (IMMUNOGLOBULIN E [IgE]) hypersensitivity reaction. Atopic DERMATITIS, commonly called eczema, tends to occur in people who have other chronic hypersensitivity conditions such as ALLERGIC ASTHMA and ALLERGIC RHINITIS. GENETIC PREDISPOSITION is the most significant risk factor for atopic dermatitis. Often there is no apparent contact allergen that sets off an atopic dermatitis attack, and symptoms may continue for several weeks to months or appear to never quite go away.

POISON IVY, POISON OAK, AND POISON SUMAC

The blistering, itchy RASH that some people develop with exposure to poison ivy, poison oak, and poison sumac is an allergic reaction to the resins on the surface of these plants. Repeated contact creates as well as intensifies sensitivity. In a highly allergic person, a reaction may occur through contact with clothing that came into contact with the resins. Contrary to popular belief, the fluid in the rash's blisters does not spread the irritation. The rash appears to spread because the person's sensitivity to the resin increases even as the allergic reaction unfolds.

Symptoms and Diagnostic Path

Allergic dermatitis, sometimes called allergic contact dermatitis, results in URTICARIA (hives) or RASH, often along with itching. BLISTER formation is common. The diagnosis is fairly straightforward when the person knows he or she has had contact with a known allergen. It is sometimes difficult to distinguish allergic dermatitis from other forms of dermatitis. In such situations ALLERGY TESTING, in which the allergist places small amounts of suspect substances in patches on the skin, can often determine the responsible allergen. Many substances, such as detergents and cleaning chemicals, can cause contact dermatitis through direct damage to the cells of the skin. Though symptoms are similar to those of allergic dermatitis, the irritation occurs

as a direct action of the substance rather than as a hypersensitivity reaction.

Treatment Options and Outlook

Treatment may include calamine lotion and cool baths or compresses to relieve itching in combination with oral ANTIHISTAMINE MEDICATIONS or CORTICOSTEROID MEDICATIONS to interrupt the immune response. Cool baths or compresses with colloidal oatmeal can soothe irritated skin. Avoiding further exposure to the allergen prevents subsequent reactions and may, over time, allow the immune response to lessen in severity.

Risk Factors and Preventive Measures

Latex, nickel, chromates, and the dyes in permanent hair coloring solutions are the most common causes of allergic dermatitis. Numerous metal objects, including stainless steel and chrome plating, contain nickel. Spandex contains latex; spandex clothing such as undergarments and athletic wear may cause hypersensitivity reaction in people who are allergic to latex. Chromates, chemicals used in tanning leather, are common in leather shoes, belts, and clothing. The allergen in permanent hair dyes is a chemical called paraphenylenediamine (PPDA), which sometimes is also present in some dyed clothing though is not commonly used in fabric dyes in the United States. The risk for allergic dermatitis is particularly high among people who work in jobs with constant exposure to these common allergens.

See also ALLERGIC ASTHMA; ALLERGIC CONJUNCTIVITIS; ATOPY; LIVING WITH ALLERGIES; OCCUPATIONAL HEALTH AND SAFETY; SKIN-ASSOCIATED LYMPHOID TISSUE (SALT); WHEAL.

allergic rhinitis A HYPERSENSITIVITY REACTION to inhaled allergens. Allergic rhinitis, also called seasonal rhinitis or hay FEVER, affects the mucous membranes inside the NOSE (nasal mucosa). Allergic rhinitis affects about 40 million adults in the United States, making it one of the most common hypersensitivity reactions. The condition tends to develop in childhood and continue through adulthood, though some people who have allergic rhinitis as children seem to outgrow their sensitivities as they become adults.

MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) infiltrates the nasal mucosa. Within the MALT are numerous mast cells, the surfaces of which harbor IMMUNOGLOBULIN E (IgE) antibodies. These antibodies react within hours to the presence of airborne allergens such as pollens. Allergic rhinitis is most common in the spring and the fall, though some people also experience symptoms in the summer, depending on what allergies they have. Allergic rhinitis is primarily a type I (IgE) hypersensitivity reaction, in which symptoms developing fairly immediately after contact with the ALLERGEN. The most common allergens associated with allergic rhinitis are tree pollens, grass pollens, and weed pollens. Other potential allergens include dust mites, pet dander, and other substances that are continuously present in the environment.

Symptoms and Diagnostic Path

The symptoms of rhinitis range from mild to debilitating. The classic symptoms occur in response to the presence of allergens and include

- nasal congestion
- itching
- sneezing
- RHINORRHEA (runny nose)

Some people also develop

- swollen, itchy, reddened eyes (ALLERGIC CONJUNCTIVITIS)
- dark circles under the eyes ("allergic shiners")
- OTITIS media (middle ear INFECTION)
- PHARYNGITIS (sore THROAT) from postnasal drip (mucus draining down the back of the throat)
- physical irritation of the nose due to frequent sneezing, blowing, and rubbing

The doctor makes the diagnosis based on the presentation of symptoms and the person's description of how the symptoms develop and how long they last.

Treatment Options and Outlook

Treatment combines avoiding the allergen when possible with medications to control symptoms.

Such medications typically include antihistamine nasal sprays, corticosteroid nasal sprays, oral ANTIHISTAMINE MEDICATIONS, and oral decongestant medications. Another classification of DRUG that is sometimes effective for allergic rhinitis is the leukotriene receptor antagonist, which blocks the action of LEUKOTRIENES (other chemicals that mediate the IMMUNE RESPONSE). The leukotriene receptor antagonist medication approved for use in the United States is montelukast (Singulair). Cromolyn sodium nasal spray targets mast cells, reducing their ability to release immune mediator chemicals such as histamine, PROSTAGLANDINS, and leukotrienes. DESENSITIZATION, commonly called allergy shots, is an option for some people. Desensitization works by exposing the IMMUNE SYSTEM to small amounts of the allergen over time to retrain the immune response to ignore the allergen.

Older antihistamine medications such as diphenhydramine (Benadryl) are very effective though cause drowsiness. Newer antihistamine medications such as loratadine (Claritin) are equally effective for most people and cause significantly less drowsiness. Antihistamines block the action of histamines, chemicals that mediate (initiate and facilitate) the processes of the immune response that result in the symptoms. Most antihistamines are available as OVER-THE-COUNTER (OTC) DRUGS that do not require a doctor's prescription. GINGER, available in various preparations, contains a mild antihistamine.

Oral decongestant medications available over the counter in the United States are pseudoephedrine and phenylephrine, though there are several OTC decongestant nasal sprays. Many OTC allergy products combine a decongestant with an antihistamine. Decongestants work by constricting the BLOOD vessels in the nasal mucosa, reducing the availability of fluid to the tissues. Chronic or long-term use of decongestants can result in rebound congestion, a condition in which the nasal membranes swell in the absence of the decongestant. Nose drops and nasal sprays containing saline (salt solution) are often as effective in relieving congestion. They work by soothing the nasal mucosa and flushing away topical irritants, including allergens.

Risk Factors and Preventive Measures

Allergic rhinitis is very common, affecting 20 percent of the American adult population. The most effective measure to reduce symptoms is to limit or eliminate exposure to the allergens that trigger the hypersensitivity response. Many people are able to mitigate symptoms by using allergy medications regularly for the duration of the allergy season.

There appears to be a GENETIC PREDISPOSITION for chronic allergic rhinitis, also called atopic rhinitis, which has more extensive symptoms that tend to be more perennial (ongoing) than seasonal. People who have atopic rhinitis have increased risk for other atopic conditions such as ALLERGIC ASTHMA (also called atopic asthma), atopic CONJUNCTIVITIS, and atopic DERMATITIS. A flare of symptoms in one atopic condition often brings on symptoms in another.

See also ALLERGIC DERMATITIS; ANTIBODY; CORTICOSTEROID MEDICATIONS; IMMUNOTHERAPY; LIVING WITH ALLERGIES; MAST CELL; SINUSITIS.

allergy An abnormal sensitivity to an ordinarily harmless substance, called an ALLERGEN, that produces a HYPERSENSITIVITY REACTION (allergic reaction) in response to the IMMUNE SYSTEM's detection of the substance's presence. A person can have an allergy to nearly any substance. Though researchers understand the mechanisms of hypersensitivity reaction, they do not know what causes the immune system to determine the substance is a potential invader. The first exposure to the substance activates an immune response that stimulates B-lymphocytes (specialized white BLOOD cells) to produce antibodies. Second and subsequent exposures engage the ANTIBODY response, in which the antibodies bind with molecules bearing the allergen to mark them for destruction.

Allergies are common. Symptoms vary according to the allergen. Some symptoms remain localized, affecting only a distinct part of the body (such as in ALLERGIC DERMATITIS or ALLERGIC RHINITIS). Others are systemic, affecting the body as a whole (such as hypersensitivity reaction to a drug or a food item). A severe hypersensitivity reaction can cause life-threatening swelling of the THROAT and airways (ANAPHYLAXIS).

See also ALLERGIC CONJUNCTIVITIS; ALLERGY TESTING; ANGIOEDEMA; ASTHMA; FOOD ALLERGIES; LIVING WITH ALLERGIES.

allergy testing Diagnostic procedures to determine the allergens responsible for HYPERSENSITIVITY REACTION. The most specific ALLERGY test is the allergy SKIN test, also called a scratch test or a patch test. For this test, the allergist uses the inside of the arm or a section of the back to expose the body to suspected allergens. The allergist places a small drop of a solution containing the ALLERGEN on a marked spot on the skin, then uses a sterile picklike instrument to scratch the surface of the skin. This exposes the IMMUNE SYSTEM to the suspected allergen. If a WHEAL (raised welt) forms on the site within 15 minutes, the test is positive for the allergen. For a typical allergy skin test, the allergist may test a number of substances at the same time, each on a different site on the skin. The allergy skin test tells the allergist the precise allergies an individual has. The allergy skin test helps the allergist strategize the most effective treatments and is necessary before DESENSITIZATION treatments.

Though it is rare, a person who has a strong allergy may have an intense reaction during an allergy SKIN test, including ANAPHYLAXIS, that requires urgent medical treatment.

A radioallergosorbent test (RAST) is a blood test that measures the amount of IMMUNOGLOBULIN E (IgE) in the BLOOD circulation when allergy symptoms are present. An amount higher than normal level of serum IgE indicates a hypersensitivity reaction. The RAST does not identify the specific allergen. There is no risk for the RAST to cause a hypersensitivity reaction because it does not expose the person to any allergens.

A food-elimination diet is the preferred allergy test to identify potential FOOD ALLERGIES. The person eliminates specific foods from his or her diet for several weeks, then reintroduces them one at a time and notes whether there are corresponding symptoms. An important part of a food-elimination diet is keeping an accurate food diary that records symptoms and other perceptions during the test. This allergy test is somewhat subjective, though often results in connecting specific foods with allergy symptoms. Another test for food allergies is the food challenge, which takes place in a hospital. The allergist gives the person certain foods, often mixed with other foods, without the person knowing, then observes and documents any symptoms that develop. There is a risk that the food challenge may cause a hypersensitivity reaction that would require immediate medical intervention; this is why the test takes place in a hospital or other emergency-ready facility.

See also ALLERGEN; ALLERGIC CONJUNCTIVITIS; ALLERGIC DERMATITIS; ALLERGIC RHINITIS; ANAPHYLAXIS.

anaphylaxis A severe HYPERSENSITIVITY REACTION (allergic reaction) in which the tissues of the throat swell, preventing air from getting to the LUNGS. Anaphylaxis, also called anaphylactic shock, is a type I hypersensitivity reaction that often develops rapidly, within minutes to an hour of exposure to the ALLERGEN. Hives, ANGIOEDEMA, and airway spasms are the most common symptoms. Some people also experience numbness or tingling of the lips and MOUTH. Though anaphylaxis can be life-threatening, with prompt and appropriate treatment it is seldom fatal.

The first line of treatment is EPINEPHRINE and antihistamine administered by injection, which immediately and effectively stop the progression of the hypersensitivity reaction. When airway (bronchial) symptoms are severe, the doctor may also administer an injectable corticosteroid medication. Swelling and related symptoms usually abate within a few minutes. Supportive treatment for symptoms often includes OXYGEN THERAPY and intravenous fluids. Most people completely recover within a few hours.

Bee stings, peanuts, intravenous penicillin, and intravenous contrast dyes for radiology procedures are the most common allergens responsible for anaphylaxis. However, anaphylaxis is possible with any ALLERGY. Anaphylaxis is fatal for about 200 Americans each year. Some people may benefit from DESENSITIZATION, depending on the allergen responsible for the hypersensitivity reaction, to mitigate the IMMUNE RESPONSE with future exposures. People who know they have severe allergies may get a doctor's prescription for an anaphylaxis

kit, which contains a prefilled syringe of injectable epinephrine.

See also BRONCHUS-ASSOCIATED LYMPHOID TISSUE (BALT); MAST CELL.

angioedema A HYPERSENSITIVITY REACTION (allergic reaction) that produces swelling and fluid accumulation beneath the surface of the SKIN, similar in appearance to URTICARIA (hives). Angioedema occurs in response to HISTAMINE release and typically affects the face, especially around the eyes and lips, and can be life threatening when it is severe or if it develops in the throat. Swelling in the form of welts may also occur on the hands and feet. Hypersensitivity reaction to ingested allergens is the most common cause of angioedema.

Difficulty BREATHING with angioedema is a medical emergency that requires immediate hospital care.

The doctor can diagnose angioedema based on the appearance of the symptoms and the person's exposure to an ALLERGEN. Treatment may include ANTIHISTAMINE MEDICATIONS; CORTICOSTEROID MEDICATIONS; or for severe symptoms, an EPINEPHRINE injection. Cool cloths applied to the sites of the angioedema may further ease discomfort. After the histamine release ends, the body reabsorbs the fluid. Relief improves as the swelling goes down, and symptoms are generally gone within three or four days. Avoiding the allergen prevents the hypersensitivity reaction and the resulting angioedema.

There is a form of angioedema, hereditary angioedema, that is an inherited genetic disorder and not a hypersensitivity reaction. Though there is similar swelling beneath the skin, there is no histamine release.

See also ANAPHYLAXIS; GENETIC DISORDERS; IMMUNE RESPONSE; LIVING WITH ALLERGIES.

antibody A unique molecule that binds with a specific ANTIGEN so the IMMUNE SYSTEM can neutralize or destroy the antigen. Antigens are molecular markers on the surfaces of cells that identify the cells to the immune system. Antibodies are the immune system's infantry, patrolling the BLOOD and LYMPH circulations and responding to fight INFECTION when invading pathogens breach the barriers intended to keep them out of the body. Every time the immune system encounters new antigens it crafts new antibodies—a distinct and unique antibody for each antigen. Though antibodies all derive from IMMUNOGLOBULIN E (IgE), each kind of antibody binds only with its specific antigen. The immune system has the capacity to produce millions of unique antibodies.

B-cell lymphocytes, a type of white blood cell (LEUKOCYTE), produce antibodies each time the immune response presents a foreign antigen. Once sensitized to a specific antigen and programmed to produce antibodies for it, the B-CELL LYMPHOCYTE becomes a plasma cell and circulates in the blood and lymph. Whenever the plasma cell encounters its antigen, it churns out antibodies and releases them into the blood and lymph. Thousands to millions of plasma cells are present in the body for each antibody the immune response generates.

The antibody response is the foundation of ANTIBODY-MEDIATED IMMUNITY, also called humoral immunity, the process by which the immune system prevents reinfection by specific pathogens. Vaccines manipulate antibody-mediated immunity by introducing weakened pathogens (such as viruses and BACTERIA) to stimulate B-cell lymphocytes to produce antibodies against them. The blood and lymph circulations then contain the antibodies though the person has never had the infection.

Blood tests for the presence of specific antibodies help doctors diagnose numerous health conditions and determine whether a person has immunity against viral infections such as RUBELLA (German measles) and infectious mononucleosis. Antibody testing is also a key step in determining the match potential between an organ transplant recipient and the donor organ.

For further discussion of antibodies within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ALLERGY; CELL-MEDIATED IMMUNITY; CELL STRUCTURE AND FUNCTION; COMPLEMENT CASCADE; GAMMAGLOBULIN; HYPERSENSITIVITY REACTION; MONOCLONAL ANTIBODIES (MABS); MONONUCLEOSIS, INFECTIOUS; ORGAN TRANSPLANTATION; PATHOGEN; VACCINE; VIRUS.

antibody-mediated immunity The mechanism through which specialized immune cells, primarily B-cell lymphocytes, carry out the IMMUNE RESPONSE to protect the body from extracellular pathogens (disease-causing entities, such as BACTERIA and other microbes, present in the BLOOD or LYMPH that have not invaded the body's cells). Antibody-mediated immunity, also called humoral immunity, encompasses the functions of ANTIBODY production and immune memory. Antibody-mediated immunity functions collaboratively with CELL-MEDIATED IMMUNITY to help protect the body from INFECTION.

Specialized B-cell lymphocytes called PLASMA cells produce antibodies, protein molecules that circulate in the blood and lymph. Exposure to antigens for which they are sensitized activates plasma cells to produce antibodies. The antibodies bind with the antigens that match their ANTIGEN receptors (molecular sites that match the configuration of the antigen). The antibody–antigen bond activates the COMPLEMENT CASCADE, a complex interaction of blood proteins (the complement system) that results in penetration and death of the foreign cell.

Antibody binding also releases various CYTOKINES (protein molecules that serve as chemical messengers) that then activate other processes in the immune response. Immune cells that may respond to these messages include macrophages, granulocytes (basophils, eosinophils, and neutrophils), and T-cell lymphocytes (notably helper T-cells [Th2 cells]). The sequence of events takes about 36 hours to unfold after the IMMUNE SYSTEM recognizes the antigen as foreign. The immune response then works to neutralize the threat.

Memory B-cells circulate in the blood and lymph for an extended period of time. They hold a "memory" imprint of specific pathogens. When the PATHOGEN again enters the body, the memory-B cells remember and immediately ramp up antibody production. This process shortcuts the usual immune response, allowing the immune system to mount a defense before the pathogen can initiate an infection.

See also B-CELL LYMPHOCYTE; CELL STRUCTURE AND FUNCTION; GRANULOCYTE; MACROPHAGE; T-CELL LYMPHOCYTE; VACCINE.

antigen A molecule that resides on the surface of a cell membrane and is capable of stimulating an IMMUNE RESPONSE. Antigen molecules are either lipoproteins (lipid and protein) or glycolipids (lipid and GLUCOSE). Each cell has numerous antigens that that identify it to the IMMUNE SYSTEM. Cells that belong to the body bear antigens that mark them as self cells; the immune system does not react to them. The antigens on cells that are foreign to the body alert the immune system to the presence of nonself cells, which activates an immune response. Foreign or nonself antigens cause the immune system to develop antibodies, unique proteins (immunoglobulins) that inactivate or destroy specific antigens.

ANTIGENS AND BLOOD TYPE

Antigens form the basis of the ABO and rhesus (Rh factor) classification for BLOOD TYPE. Antigens coat the cell membrane surface of erythrocytes (red BLOOD cells) for blood types A, B, and AB. The erythrocytes of type O blood do not have antigens. Erythrocytes may also have Rh antigens, designated as "positive" when used to identify blood type. For example, A+ erythrocytes bear type A and Rh antigens. O– erythrocytes have neither ABO antigens nor Rh antigens.

Antigen Processing

Macrophages, tissue-bound phagocytic white BLOOD cells that start life as monocytes circulating in the blood, are abundant in the LYMPH tissues. They are the immune cells that sound the alarm to the rest of the immune system that nonself antigens are present. When a macrophage encounters a foreign entity, it surrounds and ingests it. As the MACROPHAGE consumes the invader, it displays the invader's antigens on the surface of its cell membrane. This display announces the presence of the antigens to other immune cells, notably T-cell lymphocytes, which then mount a full immune response. Other cells that may serve as antigen-presenting cells include B-cell lymphocytes and dendritic cells. Once T-cell lymphocytes "read" the antigen message the macrophage displays, they respond by attacking and killing the invader. Correspondingly, B-cell

lymphocytes (PLASMA cells) generate antibodies to further target the antigen.

Antigens and Cancer

The antigens on the surface of cancer cells have become a focus of much research into early diagnosis and new treatments for cancer. Cancer cells begin as normal cells in the body, bearing self-cell antigens. As the cells change and become cancerous they develop additional antigens. Blood tests can detect some of these antigens, such as PROSTATE SPECIFIC ANTIGEN (PSA) on PROSTATE CANCER cells. Cancer researchers believe the immune response fails to recognize the mixed antigen population on cancer cells as nonself, which allows the cancer to grow.

For further discussion of antigens within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; B-CELL LYMPHOCYTE; BLOOD TRANSFUSION; CELL STRUCTURE AND FUNCTION; CLUSTERS OF DIFFERENTIATION; COMPLEMENT CASCADE; CYTOKINES; ERYTHROCYTE; HUMAN LEUKOCYTE ANTIGENS (HLAS); IMMUNOGLOBULIN; IMMUNOTHERAPY; MONOCYTE; TUMOR MARKERS.

antihistamine medications Medications that block the action of HISTAMINE, a chemical that acts on the BLOOD vessels during an IMMUNE RESPONSE to allow fluid to flood the tissues. The resulting INFLAMMATION is part of the body's means of delivering INFECTION-fighting agents to the site (such as T-lymphocytes, CYTOKINES, and antibodies). However, this response is exaggerated in a HYPERSENSITIVITY REACTION, during which histamine secretion is excessive or continues after the immune response has neutralized the triggering ANTIGEN.

Large, granulated leukocytes (white blood cells) called mast cells produce, store, and release histamine (as well as serotonin and other chemicals). Mast cells reside in the mucous membranes of the respiratory tract (nasal passages, nasal sinuses, TRACHEA, and bronchi) and the gastrointestinal tract (primarily the STOMACH). Mast cells also store and release serotonin. Histamine is primarily responsible for the inflammatory changes that result in hypersensitivity reaction (allergic reaction).

STABILIZING MAST CELLS TO PREVENT HISTAMINE RELEASE

A different therapeutic approach to managing the HISTAMINE cascade in HYPERSENSITIVITY REACTION is to regulate histamine release at the level of the mast cells, which is most effective as a treatment for ALLERGIC ASTHMA (hypersensitivity reaction of the airways). Drugs called MAST-CELL stabilizers work by preventing the granules in mast cells from releasing histamine (called degranulation) as part of the IMMUNE RESPONSE. Mast-cell stabilizers to treat allergic ASTHMA include cromolyn and nedocromil.

How These Medications Work

Antihistamines work by blocking the ability of histamine to bind with histamine receptors on the surfaces of cell membranes. Antihistamines target the two types of histamine receptors involved with the immune response: H1 and H3. H1 receptors regulate arteriole dilation and capillary permeability. Histamine causes dilation of the arterioles, the body's tiniest arteries, to increase blood flow to the tissues and increases the flow of plasma out from the capillaries into the interstitial spaces, to flood the tissues with antibodies, cytokines, PROSTAGLANDINS, and other molecules essential to the immune response.

When taken at the onset of symptoms (while histamine release is still taking place) or prophylactically (to prevent histamine release, such as to treat seasonal allergies), antihistamine medications relieve the common symptoms of ALLERGY such as itching and sneezing. However, antihistamines cannot reverse the effects of histamine release after they occur or reduce inflammation that has already developed. Antihistamine medications to treat hypersensitivity reaction are available in oral, topical, inhalation, and injection preparations. Doctors may also prescribe antihistamines to relieve NAUSEA, particularly that of motion sickness, and mild anxiety.

First-generation antihistamines, long the mainstay of treatment for allergies, are nonselective. They block both H1 and H3 receptors. H1 blocking subdues symptoms of hypersensitivity reaction. H3 receptors signal BRAIN neurotransmitters in the HYPOTHALAMUS that regulate alertness and the nau-

sea center. Antihistamine medications with H3 blocking capability thus cause drowsiness and relieve nausea as well. Second-generation antihistamine medications are selective. They block primarily H1 receptors and have little effect on H3 receptors; thus they do not generally cause drowsiness and provide little or no relief of nausea. Third-generation antihistamine medications derive from second-generation antihistamines and are purported to have fewer side effects and adverse reactions though functionally are no different. Many antihistamine medications are available in the United States as OVER-THE-COUNTER (OTC) DRUGS, sometimes in combination with a decongestant or other ingredients. Manufacturers often market OTC antihistamines as allergy-relief products. Other antihistamines require a doctor's prescription.

ANTIHISTAMINE MEDICATIONS

First-Generation (Nonselective) Antihistamines	
brompheniramine	chlorpheniramine
dexchlorpheniramine	dimenhydrinate
diphenhydramine	doxylamine
hydroxyzine	phenindamine
pheniramine	pyrilamine
triprolidine	
Second-Generation (Selective H1) Antihistamines	
acrivastine	azatadine
cetirizine	clemastine
cyproheptadine	loratadine
mizolastine	
Third-Generation (Selective H1) Antihistamines	
desloratadine	fexofenadine
levocetirizine	

Therapeutic Applications

Doctors prescribe or recommend antihistamine medications to treat ALLERGIC RHINITIS, ALLERGIC CONJUNCTIVITIS, and ALLERGIC DERMATITIS. Most of the nonselective antihistamines cause significant drowsiness; doctors prescribe or recommend them for intermittent insomnia (difficulty sleeping). Meclizine is an H3 receptor antihistamine effective for nausea and VOMITING, especially that associated with motion sickness. Meclizine has little effect on H1 receptors, however, so does not influence the immune response or relieve symptoms of hypersensitivity reaction.

Some antihistamine medications have other therapeutic applications, such as

- anxiety: hydroxyzine
- sedative and sleep aid: diphenhydramine, doxylamine, hydroxyzine
- nausea and vomiting: dimenhydrinate, diphenhydramine, hydroxyzine
- VERTIGO: dimenhydrinate, diphenhydramine
- early PARKINSON'S DISEASE: diphenhydramine

Risks and Side Effects

In general antihistamine medications cause few side effects other than drowsiness, although can raise BLOOD PRESSURE. People who take other medications to treat chronic health conditions should check with their doctors before taking antihistamines, as antihistamines can exacerbate symptoms or interfere with the actions of other drugs.

See also ANTIBODY; ARTERY; CORTICOSTEROID MEDICATIONS; CAPILLARY BEDS; GENERALIZED ANXIETY DISORDER (GAD); H2 ANTAGONIST (BLOCKER) MEDICATIONS; LIVING WITH ALLERGIES; LYMPHOCYTE; NEUROTRANSMITTER; PROTON PUMP INHIBITOR MEDICATIONS; SNEEZE.

antimitochondrial antibodies Autoantibodies the IMMUNE SYSTEM produces that attack the mitochondria within self cells. Mitochondria are the organelles (functional structures) within a cell that generate the energy the cell needs to carry out its activities. Antimitochondrial antibodies are proteins that bind with antigens (other proteins) on the inner walls of the mitochondria, blocking the ability of the mitochondria to convert oxygen to energy. The cell dies as a result.

CONDITIONS IN WHICH ANTIMITOCHONDRIAL ANTIBODIES ARE PRESENT

CIRRHOSIS	PRIMARY BILIARY CIRRHOSIS
PRIMARY SCLEROSING CHOLANGITIS	RHEUMATOID ARTHRITIS
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	THYROIDITIS

A BLOOD test called the antimitochondrial ANTIBODY (AMA) titer detects and measures antimitochondrial antibodies in the blood circulation. Their presence indicates various AUTOIMMUNE DISORDERS, notably PRIMARY BILIARY CIRRHOSIS and PRIMARY SCLE-

ROSING CHOLANGITIS, two conditions that damage the LIVER. Normally antimitochondrial antibodies are not present.

See also ANTIGEN; CELL STRUCTURE AND FUNCTION; IMMUNE RESPONSE.

antiphospholipid antibodies Autoantibodies the IMMUNE SYSTEM produces that attack phospholipids, fatty substances in the cell membranes of BLOOD cells and connective tissue cells. Antiphospholipid antibodies interfere with blood clotting (COAGULATION) and are present in a number of AUTOIMMUNE DISORDERS that affect connective tissue, such as RHEUMATOID ARTHRITIS (affecting the joints) and VASCULITIS (affecting the blood vessels). Antiphospholipid antibodies are also present in SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).

Several blood tests can detect and measure the level of antiphospholipid antibodies, reported as a titer. Antiphospholipid antibodies are not normally present. Positive findings when there are no other autoimmune conditions may indicate a diagnosis of primary antiphospholipid syndrome. The primary effect of antiphospholipid antibodies is increased blood clotting, resulting in conditions such as DEEP VEIN THROMBOSIS (DVT), TRANSIENT ISCHEMIC ATTACK (TIA), repeated miscarriage in PREGNANCY, HEART ATTACK, and STROKE.

See also ANTIBODY; ANTIGEN; ANTIMITOCHONDRIAL ANTIBODIES.

atopy A genetically predisposed HYPERSENSITIVITY REACTION. Atopy is typically chronic. The most common forms of atopy are

- atopic ASTHMA, which affects the airways (bronchi)
- atopic DERMATITIS, which affects the SKIN
- atopic rhinitis, which affects the nasal passages (nose)
- atopic CONJUNCTIVITIS, which affects the membranes that line the eyelids (conjunctiva) and the sclera (white) of the EYE

The symptoms of atopic conditions are the classic symptoms of ALLERGY, though tend to appear at the slightest exposure to allergens and linger for an extended time. Atopy is a type I or IMMUNOGLOBULIN E (IgE) hypersensitivity reaction that occurs fairly immediately after exposure to the ALLERGEN. Treatments for atopic conditions target the IMMUNE RESPONSE as well as symptom relief and may include oral and topical ANTIHISTAMINE MEDICATIONS and CORTICOSTEROID MEDICATIONS. Avoiding known or suspected allergens significantly reduces the severity of an atopic attack.

See also ALLERGIC ASTHMA; ALLERGIC CONJUNCTIVITIS; ALLERGIC DERMATITIS; ALLERGIC RHINITIS; BRONCHUS; GENETIC PREDISPOSITION; LIVING WITH ALLERGIES.

autoimmune disorders Health conditions in which the body's IMMUNE RESPONSE loses the ability to identify certain self cells and attacks them. Autoimmune disorders may produce symptoms that are localized (affect a clearly defined part of the body), systemic (affect a body system), or generalized (affect the body as a whole or across several systems). Though researchers do not know what causes the immune response to lose tolerance for certain antigens, causing it to identify self cells as nonself cells, they do know that a person who has one autoimmune disorder is at risk for developing others.

AUTOIMMUNE DISORDERS

autoimmune HEPATITIS	BULLOUS PEMPHIGOID
dermatomyositis	DIABETES (type 1)
DISCOID LUPUS ERYTHEMATOSUS (DLE)	GOODPASTURE'S SYNDROME
GRAVES'S DISEASE	Hashimoto's THYROIDITIS
INFLAMMATORY BOWEL DISEASE (IBD)	MULTIPLE SCLEROSIS
MYASTHENIA GRAVIS	PEMPHIGUS
pernicious ANEMIA	POLYMYOSITIS
REITER'S SYNDROME	RHEUMATOID ARTHRITIS
scleroderma	SJÖGREN'S SYNDROME
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	VASCULITIS

Over time the immune attacks permanently damage or destroy tissue. Autoimmune disorders are chronic; though treatment may control symptoms, it does not cure the disorder. Symptoms and outlook vary with the autoimmune disorder. Some autoimmune disorders, such as type 1 DIABETES and GRAVES'S DISEASE, are life threatening without treatment. Treatment is generally IMMUNOSUPPRESSIVE THERAPY with IMMUNOSUPPRESSIVE MEDICATIONS that block certain aspects of the immune response. Further treatment may be necessary to counter the damage the autoimmune

disorder causes, such as INSULIN therapy for diabetes. The course of disease may be unpredictable. Though autoimmune disorders tend to gradually worsen over time, many remain manageable with minimal symptoms or disruption of activities. There are no known preventive measures.

See also COMMON VARIABLE IMMUNE DEFICIENCY (CVID); COMPLEMENT CASCADE; DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS); HIV/AIDS; LIVING WITH IMMUNE DISORDERS; MULTIPLE CHEMICAL SENSITIVITY SYNDROME; PARTIAL COMBINED IMMUNODEFICIENCY (PCID).

B

B-cell lymphocyte A type of white BLOOD cell (LEUKOCYTE) responsible for ANTIBODY-MEDIATED IMMUNITY (also called humoral immunity). B-cell lymphocytes are so named because they come to maturity in the BONE MARROW (in contrast to T-cell lymphocytes, which come to maturity in the THYMUS). B-cell lymphocytes produce antibodies in reaction to the presence of antigens. The bone marrow generates millions of B-cell lymphocytes each day. Each B-cell lymphocyte is specific for a unique ANTIGEN.

B-cell lymphocytes may be memory B-cells, which "remember" specific antigens to mobilize a rapid IMMUNE RESPONSE upon detecting their presence, and PLASMA cells, which produce antibodies.

- Plasma cells generate antibodies in response to the presence of antigens.
- Memory B-cells remain in the circulation of the blood and LYMPH, carrying inactive antibodies. Each memory B-cell has antibodies specific to a particular antigen the immune response has previously encountered. When the memory B-cell encounters the antigen again, it immediately begins producing antibodies.

Health conditions that affect B-cell lymphocytes include cancers, such as certain types of LEUKEMIA and lymphoma, and acquired immune and AUTOIMMUNE DISORDERS.

For further discussion of B-cell lymphocytes within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also CELL-MEDIATED IMMUNITY; HIV/AIDS; T-CELL LYMPHOCYTE.

biological response modifier See IMMUNOTHERAPY.

bronchus-associated lymphoid tissue (BALT) Loosely organized clusters of LYMPH tissue beneath the epithelium (tissue that forms the mucous lining) of the bronchi (inner airways) in the LUNGS. These clusters of lymph tissue have preventive, protective, and cleanup responsibilities within the IMMUNE RESPONSE. They contain

- macrophages and dendritic cells, which are phagocytic cells that consume the debris of pathogens other leukocytes (white BLOOD cells) kill
- T-cell lymphocytes, which destroy PATHOGEN-bearing cells
- B-cell lymphocytes, which produce the ANTIBODY IMMUNOGLOBULIN A (IgA), that helps keep BACTERIA and viruses from adhering to mucous tissues, such as the lining of the nasal sinuses and the bronchi
- M cells (folded, M-shaped cells that engulf pathogens and transport them to phagocytes), which participate in the various stages of ANTIGEN dispensation

BALT, like collections of accessory lymphoid tissue elsewhere in the body, reinforces the presence of the IMMUNE SYSTEM in areas where the body is vulnerable to invasion of pathogens (viruses, bacteria, and other potentially harmful substances). A specific role of BALT is to provide an extra layer of immune protection to block or limit access by viruses that cause infections specific to the lungs, such as INFLUENZA and PNEUMONIA.

For further discussion of BALT within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also BRONCHUS; CELL STRUCTURE AND FUNCTION; GUT-ASSOCIATED LYMPHOID TISSUE (GALT); LEUKOCYTE; LYMPHOCYTE; MACROPHAGE; MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); NOSE-ASSOCIATED LYMPHOID TISSUE (NALT); PHAGOCYTE; PHAGOCYTOSIS; SKIN-ASSOCIATED LYMPHOID TISSUE (SALT); VIRUS.

C

cell-mediated immunity The protective mechanism through which specialized immune cells, primarily T-cell lymphocytes and natural killer (NK) cells, carry out the IMMUNE RESPONSE to protect the body from intracellular pathogens (disease-causing entities, such as viruses and parasites, that invade the body's cells). Cell-mediated immunity encompasses cytotoxic (death of invading cells) and phagocytic (consumption of cellular debris) activities. Cell-mediated immunity functions collaboratively with ANTIBODY-MEDIATED IMMUNITY to protect the body from INFECTION.

Several kinds of T-cell lymphocytes participate in cell-mediated immunity. They include

- cytotoxic T-cells, which respond directly to antigens for which they are sensitized and kill the cells that bear them
- helper T-cells (Th1 cells), also called CD-4 cells, which release CHEMOKINES in response to the presence of the antigen-bearing cells
- memory T-cells, which are essential for long-term immunity against infections such as MEASLES and POLIOMYELITIS (activated through disease or vaccination)
- suppressor T-cells, which bring the immune response to a close when the threat is gone

Macrophages set cell-mediated immunity in action when they display the antigens of a consumed cell. When these are nonself antigens, cytotoxic T-cells respond to kill other cells bearing the ANTIGEN. When the antigen is one the body has previously encountered, memory T-cells sensitized to the particular antigen rapidly convert to cytotoxic T-cells and mount a fast-strike immune response. The ability of cell-mediated immunity to rid the body of nonself-antigen-bearing cells is highly effective for controlling infection though also becomes problematic in ORGAN TRANSPLANTATION. Cell-mediated immunity, with its focus on nonself antigens, is key to GRAFT VS. HOST DISEASE and organ transplant rejection.

The NK cell, a type of granular LEUKOCYTE, does not respond to antigens. Rather, it responds to MAJOR HISTOCOMPATIBILITY COMPLEX (MHC) molecules on the surfaces of cell membranes. Attacking NK cells produce CYTOKINES that weaken the cell membrane of the targeted cells, which indirectly causes the death of the cells. NK cells also respond to tumor antigens and are particularly active in killing cancer cells. Researchers believe NK cells have a limited ability to recognize changes in cells that alter cellular identity (altered self), such as those occurring when cells turn cancerous. However, researchers do not understand the mechanisms of this recognition or to what extent NK cells are able to suppress the growth of cancer cells.

See also HYPERSENSITIVITY REACTION; MACROPHAGE; MONONUCLEAR PHAGOCYTE SYSTEM; NATURAL KILLER (NK) CELL; PARASITE; PATHOGEN; PHAGOCYTE; PHAGOCYTOSIS; T-CELL LYMPHOCYTE; VACCINE; VIRUS.

chemokines Proteins, also called chemotactic CYTOKINES, that draw or direct leukocytes to the scene of INFECTION within the body. Macrophages produce chemokines when they encounter foreign cells, instigating an IMMUNE RESPONSE. Some chemokines act as homing signals, marking the foreign cells so responding immune cells can zero in on them. Other chemokines send out biochemical "alerts" that attract circulating monocytes and lymphocytes.

Chemokines are integral in the process of angiogenesis (the development and growth of

new BLOOD vessels) that occurs when both HEALING and tumor progression (such as in cancer) takes place. Researchers are exploring ways to target chemokines as a means of shutting down angiogenesis, which has the potential to starve tumors.

See also IMMUNOTHERAPY; LEUKOCYTE; LYMPHOCYTE; MACROPHAGE; TUMOR NECROSIS FACTORS (TNFS).

clusters of differentiation A system of classifying lymphocytes according to the collections of antigens on the surface of their cell membranes, also called CD markers. Each CD has a specific role in cell signaling and communication, guiding cell function and response. CDs are critical to the normal function of the IMMUNE SYSTEM. Some of the major CDs are

- CD-1, which populates B-cell lymphocytes and macrophages and has a role in ANTIGEN presentation
- CD-2, which populates T-cell lymphocytes and natural killer (NK) cells and activates T-cells
- CD-3, which populates T-cell lymphocytes and facilitates antigen binding (the ability of T-cell lymphocytes to receive biochemical messages)
- CD-4, which populates T-helper cells (T-cell lymphocytes that direct IMMUNE RESPONSE to INFECTION) and is a key marker for monitoring the progression of HIV/AIDS
- CD-5, which populates B-cell lymphocytes that produce IMMUNOGLOBULIN M (IgM)
- CD-7, which populates T-cell lymphocytes in acute lymphocytic LEUKEMIA (ALL) and is a marker for STEM CELL leukemias
- CD-8, which populates T-suppressor cells (T-cell lymphocytes that end the immune response) and is a key marker for monitoring the progression of HIV/AIDS

CD-4 AND HIV/AIDS

CD-4 has become an important marker in tracking the progression of HIV/AIDS, as HIV-1 and HIV-2 bind with this ANTIGEN to gain access to the body. CD-4 receptors are abundant on certain T-cell lymphocytes called T-helper cells (also called T_4 cells). In health, CD-4 coordinates numerous aspects of the IMMUNE RESPONSE. When pathogens such as HIV bond with CD-4 receptors, they block the ability of CD-4 to signal other immune cells. This communication failure disrupts the IMMUNE SYSTEM's ability to mount an effective immune response. HIV also uses the T-helper cells to replicate itself, further spreading INFECTION. In combination, these events allow OPPORTUNISTIC INFECTION that can overwhelm the body.

See also ANTIBODY; CYTOKINES; HUMAN LEUKOCYTE ANTIGENS (HLAS); B-CELL LYMPHOCYTE; LYMPHOCYTE; MACROPHAGE; MAJOR HISTOCOMPATABILITY COMPLEX (MHC); MONOCLONAL ANTIBODIES (MABS); NATURAL KILLER (NK) CELL; PHENOTYPE; T-CELL LYMPHOCYTE.

colony-stimulating factors (CSFs) Molecules that stimulate the growth of leukocytes (white BLOOD cells) in the BONE MARROW. The body produces minute quantities of CSFs to regulate LEUKOCYTE production, maintaining the various types of leukocytes at appropriate levels to meet the needs of immune function. CSF production increases during INFECTION and other demands for higher quantities of white blood cells.

In the 1990s researchers isolated the genes that encode CSFs, permitting the use of recombinant technology to create synthetic versions of CSFs for therapeutic applications. Today doctors administer CSFs to rapidly restore white blood cell production after IMMUNOABLATION during the course of treatment for some forms of LEUKEMIA and certain other cancers for which BONE MARROW TRANSPLANTATION is a treatment option, and some chemotherapeutic regimens that are known to be very ablative to the white blood cells. Immunoablation uses high-DOSE CHEMOTHERAPY or RADIATION THERAPY to destroy the diseased bone marrow. During the approximately six weeks it takes for the transplanted bone marrow to begin producing new blood cells, the person has no immune function and is extremely vulnerable to infection. CSF therapy dramatically shortens this period of vulnerability, stimulating leukocyte production within days of the bone marrow transplantation.

See also CYTOKINES; GENE; HEMATOPOIESIS; IMMUNE RESPONSE; IMMUNOSUPPRESSIVE THERAPY; RECOMBINANT DNA.

common variable immunodeficiency (CVID) An immune disorder in which the IMMUNE SYSTEM lacks the ability to produce adequate antibodies to protect the body from INFECTION. Though there are normal numbers of B-lymphocytes in the BLOOD circulation, these ANTIBODY-producing cells are lacking IMMUNOGLOBULIN G (IgG), a protein essential for ANTIGEN recognition and antibody production. IgG is the foundation for most antibodies that the immune system produces.

Symptoms and Diagnostic Path

Symptoms of CVID can show up any time after about age 10 though most commonly appear in the late 20s and early 30s. Generally the person has the same type of infection repeatedly, as the immune system is not producing antibodies to protect against the infectious agent. The key symptom is a progressive pattern of recurrent or chronic infections. Infections are most commonly upper respiratory, SINUSES, THROAT, and middle EAR—typically BRONCHITIS, PNEUMONIA, PHARYNGITIS, SINUSITIS, and OTITIS media. Infections may be viral, bacterial, fungal, or parasitic. Some people also have gastrointestinal infections. The severity of infection varies among people who have CVID as well as within an individual from infection to infection. The diagnostic path includes blood tests to measure IgG and antibody levels. Immunoglobulin A (IgA) and immunoglobulin M (IgM) levels may also be low.

Treatment Options and Outlook

The main therapeutic course is reducing exposure to known infection (such as common viral infections) and treatment with ANTIBIOTIC MEDICATIONS at the first sign of infection. GAMMAGLOBULIN injections can bolster the immune system, though the gammaglobulin (which comes from blood or PLASMA donors) may not contain the specific antibodies the person needs. With effective medical management and diligent prevention efforts, most people who have CVID can enjoy relatively normal lifestyles and life expectancy.

Risk Factors and Preventive Measures

Most CVID is acquired, though researchers do not know what causes it to occur. There are no known measures for preventing CVID. CVID occurs more frequently in people who have AUTOIMMUNE DISORDERS such as RHEUMATOID ARTHRITIS or SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). Prompt diagnosis and appropriate treatment are essential for preventing substantial lung damage that can occur from recurrent infections.

See also BACTERIA; FUNGUS; HAND WASHING; LUNGS; PARTIAL COMBINED IMMUNODEFICIENCY (PCID); PARASITE; PERSONAL HYGIENE; SEVERE COMBINED IMMUNODEFICIENCY (SCID); LIVING WITH IMMUNE DISORDERS; VIRUS.

complement cascade The series of events that take place when an ANTIBODY binds with an ANTIGEN, activating the complements. Complements are proteins that participate in immune and inflammatory processes, acting primarily to kill antibody-marked cells. The biochemical interactions that take place with their activation ultimately lead to the formation of a protein structure called the terminal complement component or the membrane attack complex. The membrane attack complex penetrates the cell membrane of the antibody-marked cell. This penetration kills the cell and coats it in proteins that mark it for PHAGOCYTOSIS, the process through which LEUKOCYTE (white BLOOD cell) scavenger cells, called phagocytes, consume the debris that remains after the attacked cell dies.

There are about 30 complement proteins, also called complement factors, in the blood circulation. They remain inactive until antibody–antigen bindings or certain other immune responses activate them. Doctors classify activated complements into nine major molecular complexes identified as C1–C9. C1–C4 form the preliminary pathways leading to the formation of the membrane attack complex. C5–C9 collectively form the membrane attack complex. Other proteins interact with the complements to keep their actions in check. Disintegration of the complement complexes begins immediately after their activation to prevent them from damaging other cells.

Blood tests can measure complement activity in the body. Complement activity is often increased in the presence of cancer and decreased with certain AUTOIMMUNE DISORDERS such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). Complement activity also diminishes in GRAFT VS. HOST DISEASE.

Deficiencies in various complement complexes increase susceptibility to INFECTION and the risk for disorders of the immune system. People who have deficiencies in the preliminary complement cascade pathways that unfold before the formation of the membrane attack complex are particularly vulnerable to infections such as MENINGITIS and PNEUMONIA. Certain of the pathogens that can cause these infections are encapsulated—viruses and BACTERIA that enclose themselves in capsules, or envelopes. The purpose of this encapsulation is to protect the pathogen against the body's defense mechanisms. When defects weaken those mechanisms, the pathogens gain advantage in establishing themselves—and infection—within the body.

Other complement deficiencies are common in SLE and some forms of VASCULITIS (disorders involving autoimmune INFLAMMATION of blood vessels). Treatment focuses on the symptoms of the consequential disorders, notably aggressive antibiotic therapy for infection. There are, as yet, no treatments to correct complement deficiencies. Doctors recommend meningococcal, pneumococcal, and *Haemophilus influenzae* VIRUS vaccinations for people who have complement deficiencies, to bolster the IMMUNE SYSTEM's ability to protect against infections from these pathogens.

For further discussion of the complement cascade within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBIOTIC MEDICATIONS; IMMUNE RESPONSE; MONONUCLEAR PHAGOCYTE SYSTEM; ORGAN TRANSPLANTATION; PHAGOCYTE; VACCINE.

corticosteroid medications Anti-inflammatory medications that suppress INFLAMMATION and other aspects of the IMMUNE RESPONSE. Corticosteroid medications are synthetic variations of the body's natural HORMONE CORTISOL, which the ADRENAL GLANDS produce. Corticosteroids come in injectable, oral, inhalant, and topical preparations.

How These Medications Work

Corticosteroid medications work by blocking a number of the pathways in the immune response, key among them those that produce inflammation. They suppress the COMPLEMENT CASCADE, activation of antibodies, and production of eosinophils (white BLOOD cells that become abundant in a HYPERSENSITIVITY REACTION). Eosinophils are also important for fighting INFECTION, so suppressing them reduces the IMMUNE SYSTEM's ability to mount an effective defense when infection occurs. Corticosteroids also act to suppress MAST CELL release of HISTAMINE, LEUKOTRIENES, and PROSTAGLANDINS—biochemicals that facilitate inflammation.

There are three general types of corticosteroids, classified according to how they act in the body: glucocorticoids, mineralocorticoids, and ANDROGENS (the sex hormones). Glucocorticoids have the strongest anti-inflammatory action; most corticosteroid drugs are either glucocorticoids or a combination of glucocorticoid and mineralocorticoid. ALDOSTERONE, another hormone the adrenal cortex produces, is a mineralocorticoid used therapeutically as hormone replacement to treat ADDISON'S DISEASE (a condition in which the adrenal glands fail). However, aldosterone and other mineralocorticoids alone have very little anti-inflammatory action.

CORTICOSTEROID MEDICATIONS

betamethasone	cortisone
desoximometasone	fluticasone
dexamethasone	hydrocortisone
methylprednisolone	mometasone
prednisolone	prednisone
triamcinolone	

Therapeutic Applications

Doctors may prescribe corticosteroid medications to relieve symptoms of moderate to severe hypersensitivity reaction, to prevent GRAFT VS. HOST DISEASE in bone marrow transplant recipients, and to treat chronic inflammatory conditions such as severe OSTEOARTHRITIS, RHEUMATOID ARTHRITIS, ANKYLOSING SPONDYLITIS, PSORIASIS, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and INFLAMMATORY BOWEL DISEASE (IBD). Corticosteroids in nasal sprays and inhalant forms are effective treatments for ALLERGIC RHINITIS and ALLERGIC ASTHMA. Systemic corticosteroid medications are also among the treatment options for severe asthma and certain other chronic inflammatory lung conditions.

It is important to take or use corticosteroid products correctly, particularly inhalants and nasal

sprays. Generally, corticosteroids are most effective when taken on a regular schedule to prevent the inflammatory process from developing, though they also can help suppress an inflammatory response after it begins. Because long-term corticosteroid therapy also suppresses the function of the adrenal glands, the body stops producing cortisol and becomes dependent on the external source of corticosteroids (the medication). It is important to reduce the dose over time (taper) when stopping a systemic corticosteroid, to allow the adrenal glands to resume cortisol production. Suddenly stopping systemic corticosteroid therapy can result in a rebound syndrome, with symptoms of inflammation, PAIN, and FEVER.

Risks and Side Effects

Side effects are uncommon with short-term systemic (oral and injection forms), inhalation, or topical corticosteroid use. However, corticosteroids tend to be less effective with repeated or chronic use. Injected corticosteroids, such as to treat inflammation in joints, can cause tissue damage over time. Doctors generally limit corticosteroid injections to prevent such damage. Long-term use of inhaled corticosteroids is often irritating to the tissues of the NOSE or THROAT. Long-term topical corticosteroids can cause thinning and darkening of the SKIN.

Long-term systemic corticosteroid therapy, such as for immunosuppression or to treat severe autoimmune disorders, has numerous side effects that require close monitoring to maintain optimal health. Key among them are increased risks for type 2 DIABETES and OSTEOPOROSIS. Systemic corticosteroids alter the body's hormonal balance and interactions, affecting numerous endocrine functions such as regulatory mechanisms for INSULIN–GLUCOSE METABOLISM and calcium balance in the bones. Systemic corticosteroids also influence thyroid hormones, which may alter overall metabolism to result in side effects such as rapid weight gain (with a characteristic rounded face) and excessive tiredness. Some people experience mood swings, mood disorders, DEPRESSION, or GENERAL ANXIETY DISORDER (GAD) when taking long-term corticosteroid therapy, a consequence of the influence corticosteroids exert on BRAIN neurotransmitters.

Because they suppress the immune response and LEUKOCYTE (white blood cell) production, systemic corticosteroids also increase the risk for infection. Chronic COLDS, URINARY TRACT INFECTION (UTI), CANDIDIASIS (yeast infection), and wounds that are slow to heal are common with long-term systemic corticosteroid therapy. Early treatment with ANTIBIOTIC MEDICATIONS or ANTIFUNGAL MEDICATIONS can help the body fight such infections. Systemic corticosteroids interact with numerous other medications and, because they cause sodium and fluid retention, may increase BLOOD PRESSURE or cause HYPERTENSION.

See also BONE; CUSHING'S SYNDROME; DRUG INTERACTION; 5-AMINOSALICYLATE (5ASA) MEDICATIONS; NEUROTRANSMITTER; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); OPPORTUNISTIC INFECTION; ORGAN TRANSPLANTATION; PSYCHOSIS; THYROID GLAND; WOUND CARE.

cytokines A large family of proteins that mediate and regulate the IMMUNE RESPONSE. Leukocytes (white BLOOD cells) produce cytokines. There are more than 100 cytokines, which may act independently or synergistically with other cytokines. Among the actions of cytokines are cell homing and direction (drawing leukocytes to the site of INFECTION or injury), INFLAMMATION response, and stimulation of the numerous molecules that participate in the immune response. Cytokines may act on the cells that produce them (autocrine activity), on cells in proximity to them (paracrine activity), or on cells throughout the body (endocrine activity).

MAJOR TYPES OF CYTOKINES

CHEMOKINES	COLONY-STIMULATING FACTORS (CSFS)
ERYTHROPOIETIN (EPO)	INTERFERONS
INTERLEUKINS	LYMPHOKINES
MONOKINES	TUMOR NECROSIS FACTORS (TNFS)

See also ANTIBODY; ANTIGEN; CELL-MEDIATED IMMUNITY; HISTAMINE; HORMONE; LEUKOCYTE; LEUKOTRIENES.

D

desensitization A therapeutic method in which gradual exposure to an ALLERGEN builds up the body's tolerance for the allergen, diminishing the IMMUNE RESPONSE to encountering it. IMMUNOGLOBULIN E (IgE) is primarily responsible for the symptoms associated with type I HYPERSENSITIVITY REACTION (allergic reaction), initiating the release of histamines, LEUKOTRIENES, and PROSTAGLANDINS. These substances induce INFLAMMATION (swelling), itching, sneezing, coughing, and other physiologic responses that represent the body's attempt to rid itself of the offending substance. Desensitization gradually activates an immunoglobulin G (IgG) ANTIBODY that binds, instead of IgE, with the allergen. Because IgG does not activate mast cells, the binding produces none of the symptoms that characterize a type I hypersensitivity reaction.

In desensitization the allergist injects the person with very small amounts of the allergen ("allergy shots") regularly over a period of three to five years. Relief is generally apparent in about a year. Approximately 80 percent of people who have seasonal allergies respond to desensitization, bringing their hypersensitivity reactions within tolerable parameters or eliminating them entirely. Desensitization, sometimes called allergy IMMUNOTHERAPY, is also highly effective for allergies to pet dander (especially cats), molds, and insect stings. Desensitization may be a therapeutic option for severe FOOD ALLERGIES that are difficult to manage by avoiding the food.

Desensitization injections carry the risk for instigating a severe hypersensitivity reaction including ANAPHYLAXIS, though this is rare. Some people experience temporary discomfort with the shots. Most people who undergo desensitization treatment have few side effects, however, and find the long-term benefit of reduced hypersensitivity reaction greatly improves their QUALITY OF LIFE.

See also ALLERGIC ASTHMA; ALLERGIC CONJUNCTIVITIS; ALLERGIC RHINITIS; ALLERGY; ALLERGY TESTING; ASTHMA; COUGH; HISTAMINE; LIVING WITH ALLERGIES; MAST CELL; SNEEZE.

disease-modifying antirheumatic drugs (DMARDs) Medications that alter the IMMUNE RESPONSE slow or stop the progression of certain degenerative, AUTOIMMUNE DISORDERS. The most common use of DMARDs is to treat RHEUMATOID ARTHRITIS. DMARDs provide relief from symptoms such as INFLAMMATION and PAIN, and in many people also reduce the JOINT deformities associated with rheumatoid arthritis and other degenerative conditions that result from the same disease process (such as ANKYLOSING SPONDYLITIS).

DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS)

anti-TUMOR NECROSIS FACTORS (TNFS)	azathioprine
chloroquine	cyclophosphamide
cyclosporine	etanercept
gold salts	hydroxychloroquine
infliximab	leflunomide
methotrexate	penicillamine
sulfasalazine	

How These Medications Work

DMARDs work by altering or suppressing the immune response. Some of the DMARDs are immunosuppressive CHEMOTHERAPY drugs (such as methotrexate and cyclosporine), though researchers do not fully understand how they work to reduce autoimmune inflammation. Other DMARDs are antimalarial medications that suppress immune function by blocking the action of

enzymes involved in the inflammatory process. Anti-TNFs are MONOCLONAL ANTIBODIES (MABS) that block the release of TUMOR NECROSIS FACTORS (TNFs), CYTOKINES that influence inflammation during the immune response.

Therapeutic Applications

Because DMARDs can have significant and serious side effects, doctors prescribe them when other therapies are no longer effective. The most common use of DMARDs is to treat rheumatoid arthritis. Doctors also may prescribe DMARDs to treat another degenerative autoimmune arthritis, ankylosing spondylitis, and sometimes to treat other autoimmune conditions such as MYASTHENIA GRAVIS and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).

Risks and Side Effects

DMARDs can have significant and harmful side effects including DIARRHEA, RASH, ANEMIA, LEUKOPENIA, and increased risk for INFECTION, particularly OPPORTUNISTIC INFECTION, as a consequence of immunosuppression. Methotrexate can cause irreversible CIRRHOSIS and lung damage. A rare and potentially fatal adverse reaction to methotrexate is TOXIC EPIDERMAL NECROLYSIS (also called Stevens-Johnson syndrome). Chloroquine and hydroxychloroquine can cause vision disturbances and RETINOPATHY (permanent damage to the RETINA, resulting in VISION IMPAIRMENT).

DMARDs may also interfere with the actions of other medications. It is important to check with the doctor before using any additional medications, incuding over-the-counter products. Because of the potential risks these side effects have, doctors prescribe most non-MAb DMARDs for people whose conditions are not responding to other treatments.

See also CORTICOSTEROID MEDICATIONS; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS).

F

5-aminosalicylate (5ASA) medications Drugs taken to treat INFLAMMATORY BOWEL DISEASE (IBD), an autoimmune disorder that causes mild to severe INFLAMMATION and irritation to the COLON (bowel). People who have IBD typically experience alternating periods of exacerbation and REMISSION; in severe IBD the symptoms are often debilitating. The aminosalicylates, or 5ASAs, appear to work by suppressing the local IMMUNE RESPONSE in the mucosal lining of the SMALL INTESTINE and COLON.

Though researchers do not fully understand what causes IBD, they do know there are high levels of LEUKOTRIENES and PROSTAGLANDINS in the BLOOD circulation when IBD flares up. Researchers believe the 5ASA medications block these biochemicals from release, thus inhibiting inflammation. These drugs may also block the actions of TUMOR NECROSIS FACTORS (TNFS), CYTOKINES that also participate in the inflammatory response.

5-AMINOSALICYLATE (5ASA) MEDICATIONS

balsalazide (Colazal)
mesalamine (Asacol, Canasa, Pentasa, Rowasa)
olsalazine (Dipentum)
sulfasalazine (Azulfidine)

The 5ASAs are most effective when administered via rectal suppository or ENEMA, or by absorption-delayed oral medications (drugs that are specially coated to dissolve in the SMALL INTESTINE rather than the STOMACH) as these ROUTES OF ADMINISTRATION deliver the drug directly to the involved tissues. Pharmacologically, the 5ASAs are similar to aspirin. The most common side effects include HEADACHE, NAUSEA, and RASH (which occur most frequently with sulfasalazine and not so much with the other 5ASAs). The 5ASAs are effective for treating symptoms during exacerbations as well as for extending remission (preventing symptoms from reemerging).

See also AUTOIMMUNE DISORDERS; CORTICOSTEROID MEDICATIONS; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS).

food allergies Hypersensitivity reactions to consumed foods. Food allergies affect about nine million Americans, two thirds of them children under the age of six. Allergies to peanuts, milk, wheat, shellfish, strawberries, and eggs are among the most common. Some people are allergic to preservatives or other substances used to prepare foods. Children tend to outgrow many food allergies; however, many adults develop food allergies later in life.

Unpleasant responses—such as STOMACH irritation, FLATULENCE (intestinal gas), and episodes of DIARRHEA—to certain foods are common but are not necessarily food allergies. An ALLERGY results in the activation of antibodies that triggers a HYPERSENSITIVITY REACTION, an excessive IMMUNE RESPONSE in which the IMMUNE SYSTEM responds to a particular food as though it were a harmful substance. The COMPLEMENT CASCADE floods the BLOOD circulation with antibodies, mast cells release HISTAMINE and PROSTAGLANDINS, and various types of leukocytes mobilize to attack the ALLERGEN.

Though some symptoms may be the same—such as stomach upset and diarrhea—the difference between food intolerance and food allergy can literally be life threatening: ANAPHYLAXIS, the most severe kind of hypersensitivity reaction, is an ever-present danger with food allergies. Of particular concern are ingredients that may not be obvious, such as peanut oil or soy, and may be present in processed foods as cross-contaminants.

Symptoms and Diagnostic Path

A hypersensitivity reaction to a food produces symptoms that may include

- itching and swelling around the face, on the lips, and in the MOUTH
- nasal congestion
- wheezing or difficulty BREATHING
- sensation of a lump in the THROAT
- gastrointestinal PAIN (resulting from swelling in the intestinal mucosa)
- moderate to extensive diarrhea

More generalized symptoms such as SKIN rash, hives (URTICARIA), and ANGIOEDEMA are also possible. Symptoms may occur within minutes to 2 hours after eating the food. Anaphylaxis may develop with any hypersensitivity reaction, even when previous reactions have been mild.

ANAPHYLAXIS is a medical emergency that requires immediate treatment from a doctor. Tingling and swelling of the lips, tongue, and THROAT 20 to 60 minutes after eating a food for which there could be an allergy are possible indications of anaphylaxis.

When there is a clear connection between a specific food and a hypersensitivity response, identifying the allergen is fairly straightforward. When the connection is not clear, the diagnostic path can be arduous and may include

- blood tests to measure IMMUNOGLOBULIN E (IgE) levels
- ALLERGY TESTING with suspect substances
- elimination diet

The elimination diet involves removing suspected foods or foods that are common allergens from the diet, usually for two weeks, and then reintroducing them one at a time until symptoms recur. The last food reintroduced is the likely allergen. An elimination diet is appropriate only for people who have mild to moderate hypersensitivity reactions. The risk for anaphylaxis is too great to use the elimination diet approach in people who have had severe allergy symptoms such as wheezing, breathing difficulty, or urticaria (hives). No single diagnostic approach works for all food allergies; diagnosis becomes a process of drawing conclusions based on symptoms.

COMMON FOOD ALLERGIES

cow's milk	eggs
peanuts	shellfish (lobster, shrimp, crab)
soy	strawberries
tree nuts (almonds, cashews, walnuts, pecans)	wheat (including flour)

Treatment Options and Outlook

A moderate hypersensitivity reaction may require treatment with ANTIHISTAMINE MEDICATIONS; a serious reaction may require a course of oral CORTICOSTEROID MEDICATIONS to halt the immune response and relieve the discomfort of the symptoms. Many hypersensitivity reactions to foods produce mild symptoms that go away without treatment. A doctor should evaluate symptoms that do not improve within a few days.

The most effective long-term treatment is to avoid the allergen. This is not always as easy as it sounds because often variations of the allergen are ingredients in prepared or baked foods. Peanuts, eggs, milk, soy, and wheat are common in many foods. Cross-contamination is also a concern, particularly among processed foods manufactured in facilities that use various ingredients in different products. An ice cream manufacturer may make a flavor that has nuts, for example, and then use the same equipment to make a flavor that does not have nuts. Even residue not visible to the eye can be sufficient to cause a hypersensitivity reaction in someone who is highly allergic. Labels on packaged foods include information about whether the product comes from a facility in which cross-contamination is possible. People who have food allergies must ask about obvious as well as hidden ingredients when eating away from home.

DESENSITIZATION (allergy shots) is a therapeutic option for people who have allergies to foods that are especially common or who have severe hypersensitivity reactions. Though it takes up to two years for desensitization to reach its maximum effectiveness, most people notice a reduced hypersensitivity reaction within six months.

Risk Factors and Preventive Measures

People who have other allergies or who have family members who have food allergies are more likely to develop food allergies. There are no measures to prevent allergies, food or otherwise. Identifying and avoiding foods that cause hypersensitivity reactions are the most effective methods for preventing those reactions and their unpleasant symptoms. Many people who have food allergies are able to manage them by carefully reading product labels and asking about ingredients when eating away from home.

See also ANTIBODY; ANTIGEN; BREATH SOUNDS; CARBOHYDRATE INTOLERANCE; CELIAC DISEASE; FOODBORNE ILLNESSES; LACTOSE INTOLERANCE; LEUKOCYTE; LIVING WITH ALLERGIES; MAST CELL.

gammaglobulin A solution of immunoglobulins collected from the PLASMA of donated BLOOD or from donated plasma. The highest concentration is of IMMUNOGLOBULIN E (IgE). Health-care providers administer gammaglobulin by intramuscular or intravenous injection to provide rapid immune protection for exposure to infectious diseases such as HEPATITIS. Though the protection is temporary, it helps prevent INFECTION until the person's IMMUNE SYSTEM can produce the necessary antibodies. Gammaglobulin is the treatment of choice when there is widespread public exposure to infectious diseases, such as may occur in schools and day-care centers.

See also ANTIBODY; ANTIGEN; IMMUNITY.

graft vs. host disease A life-threatening condition in which the immune cells (leukocytes and lymphocytes) contained in allogeneic transplanted BONE MARROW (the graft, from a donor source) produce antibodies that attack other organs in the organ transplant recipient's body (the host). BONE MARROW TRANSPLANTATION (or BLOOD STEM CELLtransplantation) is the primary treatment for cancers of the BLOOD such as LEUKEMIA, lymphoma, and MULTIPLE MYELOMA. Doctors may also use bone marrow transplantation to treat some types of cancer that do not respond to other therapies, severe aplastic ANEMIA, and severe SICKLE CELL DISEASE.

Graft vs. host disease is not a threat with autologous (self) bone marrow transplantation, which re-infuses blood stem cells previously withdrawn from the person. The condition occasionally develops after solid ORGAN TRANSPLANTATION and in IMMUNOCOMPROMISED people who receive BLOOD TRANSFUSIONS.

The immune cells of the transplanted bone marrow generate antibodies that commonly attack the recipient's LIVER, gastrointestinal tract (especially the STOMACH and SMALL INTESTINE), and SKIN. Damage can be rapid and severe. When the condition involves multiple organs, as is common, catastrophic multiple system failure is very possible. Graft vs. host disease accounts for more deaths after 100 days past the bone marrow transplantation than any other cause, including the cancer under treatment.

Symptoms and Diagnostic Path

Acute graft vs. host disease occurs within 100 days after the transplantation. About 30 percent of bone marrow transplant recipients experience acute symptoms, which may include

- skin RASH
- DIARRHEA
- INFECTION

Chronic graft vs. host disease develops or continues beyond 100 days from transplantation, though typically chronic disease tends to first manifest between 3 and 12 months after the transplant. The perpetual attacks that are the hallmark of chronic graft vs. host disease result in fibrotic (SCAR-related) changes to the skin, liver, and LUNGS. About 70 percent of people who receive bone marrow transplants experience some degree of chronic symptoms, which typically include

- dry, itchy skin
- discolored or taut skin
- HAIR loss or graying
- weight loss
- shortness of breath with exertion (DYSPNEA)

- chronic fatigue
- dry eyes and MOUTH

The diagnostic path includes blood tests to measure blood cell types and counts, ANTIBODY levels, and liver enzymes. In particular, CD-4+ and CD-8+ T-lymphocytes are abundant. Tissue biopsies also show evidence of damage due to the immune attack. Doctors classify graft vs. host disease into four stages, according to the severity of symptoms; stage 1 is the mildest and stage 4, the most severe.

Treatment Options and Outlook

At present the most successful treatment is IMMUNOSUPPRESSIVE THERAPY. Ideally, prophylactic immunosuppression prevents graft vs. host disease. When symptoms occur, immunosuppression can minimize the consequences and limit damage. Immunosuppression itself carries significant risk, however. The risk for infection, especially an OPPORTUNISTIC INFECTION the IMMUNE SYSTEM could normally keep at bay, is very high. CORTICOSTEROID MEDICATIONS, the cornerstone of immunosuppressive therapy, cause serious side effects with long-term, systemic use. As well, some immunosuppressive agents are chemotoxic (they work by killing cells) and have harmful side effects. The balance between sufficient immune suppression and adequate immune function is delicate.

Other treatment options include MONOCLONAL ANTIBODIES (MABS), which bind with the ANTIGEN receptors on the cell membrane surfaces of the cells in the organ. However, the body may develop antibodies against the MAbs. Though the first treatment is successful, subsequent efforts with the same MAbs will initiate an immune attack against the MAbs. A number of clinical trials are exploring investigational treatments for graft vs. host disease. A key challenge in treatment is that, although doctors fully understand what happens during graft vs. host disease, the mechanisms by which events occur remain unknown.

Risk Factors and Preventive Measures

Anyone who has bone marrow transplantation is at risk for graft vs. host disease. Optimal matching of HUMAN LEUKOCYTE ANTIGENS (HLAS) before trans-

ACUTE GRAFT VS. HOST DISEASE STAGING

Stage	Degree of Severity	Symptoms
1	mild	SKIN RASH affecting less than 25 percent of the skin surface, often starting on the hands and feet no other symptoms
2	moderate	skin rash affecting more than 25 percent of the skin surface mild gastrointestinal discomfort and DIARRHEA mild JAUNDICE
3	severe	extensive SUNBURN-like rash over most of the body STOMACH discomfort, abdominal cramping, diarrhea frequent or chronic INFECTION nutritional deficiencies moderate jaundice and LIVER dysfunction
4	life threatening	skin blisters and peeling skin over most of the body gastrointestinal PAIN bloody diarrhea severe jaundice and significant liver dysfunction or LIVER FAILURE serious INFECTION or OPPORTUNISTIC INFECTION malabsorption of NUTRIENTS

plantation provides the most successful circumstance for preventing graft vs. host disease. When precise HLA matching is not possible, screening for and selectively removing some T-cell lymphocytes (CD-4+ and CD-8+) from the donor organ that carry antibodies likely to attack the recipient can reduce the risk for graft vs. host disease. The risk for graft vs. host disease is also higher for people who receive blood stem cells extracted from donated blood (rather than from bone marrow donation), except cord stem cells extracted from umbilical blood.

See also CLUSTERS OF DIFFERENTIATION; LEUKOCYTE; LIVING WITH IMMUNE DISORDERS; LYMPHOCYTE; MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); STEM CELL; STEM CELL THERAPY; SURGERY BENEFIT AND RISK ASSESSMENT.

granuloma An accumulation of granulocytes (also called polymorphonuclear leukocytes [PMNs]) and other cells that contain and enclose an area of INFLAMMATION at the site of cell injury, usually due to INFECTION. The effect is to "wall off" the area so the infection cannot spread. The resulting construction is fibrous (SCAR-like). Over time the PATHOGEN causing the infection within the granuloma dies but the granuloma remains. Granulomas may form anywhere in the body. CYTOKINES are instrumental in facilitating the process of granuloma formation, directing the actions of the involved immune cells.

Granulomas in the LUNGS commonly result from HISTOPLASMOSIS and other fungal infections. Granuloma inguinale is a sexually transmitted disease (STD). Granulomas are also characteristic of TUBERCULOSIS, Hansen's disease (leprosy), and SARCOIDOSIS. Any underlying infectious disease requires appropriate treatment. The doctor may surgically remove granulomas that cause discomfort or are unsightly. The granuloma itself usually causes no problems and does not require treatment.

See also FUNGUS; GRANULOCYTE; LEUKOCYTE; PHAGOCYTE; PHAGOCYTOSIS; SEXUALLY TRANSMITTED DISEASES (STDS).

gut-associated lymphoid tissue (GALT) Loosely organized, nonencapsulated clusters of LYMPH tissue beneath the epithelium (tissue that forms the mucous lining) of the gastrointestinal tract from the ESOPHAGUS to the COLON. T-cell lymphocytes, B-cell lymphocytes, and macrophages primarily inhabit GALT. The role of GALT is to block NORMAL FLORA BACTERIA (bacteria that are normally present in the gastrointestinal tract to aid digestion) from penetrating into other tissues or the BLOOD circulation. GALT also helps prevent gastrointestinal viruses from causing INFECTION. The presence of GALT in the lining of the STOMACH increases with aging. GALT also includes the small, nodelike lymphoid structures called PEYER'S PATCHES that pepper the SMALL INTESTINE. Peyer's patches intensify the presence of the IMMUNE SYSTEM and are the sites of much ANTIBODY activity from B-lymphocytes.

See also LYMPH NODE; LYMPHOCYTE; MACROPHAGE; MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); NOSE-ASSOCIATED LYMPHOID TISSUE (NALT); PATHOGEN; PHAGOCYTE; PHAGOCYTOSIS; SKIN-ASSOCIATED LYMPHOID TISSUE (SALT); VIRUS.

H

hay fever See ALLERGIC RHINITIS.

healing The processes and mechanisms by which the body repairs itself. Healing represents complex and cascading interactions among various of the body's systems and mechanisms. Among the first to respond are the COAGULATION cascade, to stop bleeding, and the IMMUNE RESPONSE, which mobilizes T-cell lymphocytes, macrophages, antibodies, the COMPLEMENT CASCADE, and the release of CYTOKINES and PROSTAGLANDINS. Fibroblasts (cells that build collagen) converge at the site about 48 hours after the injury occurs to begin construction of SCAR tissue. After about six weeks the healing process turns its focus to remodeling the collagen tissue, restoring the tissues at the site of the injury to relatively normal structure and appearance. This final phase of healing lasts six months to two years, depending on the extent of the injury.

Disease processes influence healing as well. Chronic conditions such as DIABETES and PERIPHERAL VASCULAR DISEASE (PVD), themselves likely the result of inflammatory dysfunction of some sort, damage the fine networks of nerves and BLOOD vessels that intertwine through the tissues, limiting the ability of these structures to carry signals (nerves) and transport molecules and cells vital to immune function (blood vessels). Serious injury—whether from disease process, trauma, or major surgery—affects endocrine and hormonal activity throughout the body, which influence the rate and processes of healing. Serious injury temporarily stuns the THYROID GLAND, for example, resulting in reduced production of thyroid hormones and consequential slowing of METABOLISM (EUTHYROID SICK SYNDROME).

Although researchers can map the physiologic steps of healing, much of healing remains a mystery. Researchers do not fully understand what starts, regulates, and ends the healing process. Many integrations across neurologic, endocrine, and immune functions are factors in healing. Some researchers are exploring connections between emotions and the numerous biochemical substances that are key to the healing process. Researchers know, for example, that emotional stress influences the release of numerous hormones in the body and the release of these hormones—such as the hormone CORTISOL, a powerful immunosuppressant—directly affects the functions of the IMMUNE SYSTEM. Research has shown that pain is a stressor and affects the rate of healing. Studies continue to explore the relationship between the mind and healing.

See also AYURVEDA; HORMONE; INTEGRATIVE MEDICINE; MIND–BODY INTERACTIONS; PATHOGEN; REIKI; STRESS RESPONSE HORMONAL CASCADE; TRADITIONAL CHINESE MEDICINE (TCM); WOUND CARE.

histamine A chemical that acts as an IMMUNE RESPONSE mediator. Large, granulated leukocytes called mast cells, which reside in the mucous membrane lining of the respiratory and gastrointestinal tracts, store histamine in their granules and release it during the immune response. Mast cells are most abundant in the nasal passages (including the SINUSES), the TRACHEA, and the bronchi. Histamine receptors on the surfaces of cell membranes determine how histamine affects the cell. ANTIHISTAMINE MEDICATIONS, the cornerstone of treatment for type I HYPERSENSITIVITY REACTION (allergic reaction), work by blocking histamine receptors.

Though there is only one form of histamine, its release can activate any of three types of histamine receptors: H1, H2, and H3. CYTOKINES,

PROSTAGLANDINS, and other biochemical messengers determine histamine release and what histamine binding will occur. Each histamine receptor regulates a different response:

- H1 receptors are on cell membrane surfaces of arteriole and capillary cells. H1 binding causes the arterioles to dilate (open) and the capillaries to increase the permeability of their walls. The effect of these actions is to allow additional fluid to seep from these blood vessels into the interstitial spaces (spaces between cells). The fluid floods the cells with INFECTION-fighting molecules, notably antibodies and cytokines. IMMUNOGLOBULIN E (IgE) binds with antigens and allergens, triggering H1 release. H1 is primarily responsible for type I hypersensitivity reactions such as ALLERGIC RHINITIS and ALLERGIC ASTHMA. Common antihistamine medications that block H1 receptor binding include diphenhydramine, chlorpheniramine, and hydroxyzine.
- H2 receptors are in parietal cells of the STOMACH. H2 binding acts to increase the flow of gastric acid in the stomach. Excessive secretion of histamine binding with H2 receptors is primarily responsible for GASTROESOPHAGEAL REFLUX DISORDER (GERD). Medications to limit histamine secretion and H2 receptor binding include H2 ANTAGONIST (BLOCKER) MEDICATIONS such as cimetidine and ranitidine.
- H3 receptors are neuroreceptors in the CENTRAL NERVOUS SYSTEM with high concentration in the areas of the HYPOTHALAMUS that regulate alertness. H3 binding decreases NEURON (NERVE cell) secretion of histamine, serotonin, acetylcholine, EPINEPHRINE, and NOREPINEPHRINE. The effect is to reduce alertness, which takes place as a natural aspect of the circadian cycle (body's rhythm of sleep and wakefulness). These neurotransmitters also affect the NAUSEA center. The antihistamine medications doxylamine and hydroxyzine are highly effective H3 receptor blockers.

Doctors typically consider only H1 receptor binding in the context of the immune response and focus primarily on whether its actions to initiate INFLAMMATION are helpful or counterproductive.

See also ALLERGEN; ANTIBODY; ANTIGEN; LEUKOCYTE; LEUKOTRIENES; MAST CELL; NEURORECEPTOR; NEUROTRANSMITTER; PROTON PUMP INHIBITOR (PPI) MEDICATIONS.

human leukocyte antigens (HLAs) Unique proteins (antigens) present on every nucleated cell (cell that has a nucleus) in the body. Also called histocompatibility locus antigens, HLAs allow the IMMUNE SYSTEM to identify cells as self (belonging to the body). Genes on CHROMOSOME 6, in a region called the MAJOR HISTOCOMPATIBILITY COMPLEX (MHC), regulate HLAs. Each person has unique HLAs. The nomenclature (naming convention) for HLAs identifies the ALLELE and GENE locus (position on the chromosome), designating the former with a letter and the latter with a number.

HLAs have various immune roles, including identification of self and nonself cells. This function makes HLAs of crucial importance in ORGAN TRANSPLANTATION. Incompatibility in HLAs can result in GRAFT VS. HOST DISEASE and rejection of the transplanted organ. IMMUNOSUPPRESSIVE THERAPY to subdue the IMMUNE RESPONSE in people who have organ transplants in part targets HLAs. Some research suggests that HLAs also may play crucial roles in the development of AUTOIMMUNE DISORDERS such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), MULTIPLE SCLEROSIS, and SJÖGREN'S SYNDROME.

Though there are nearly endless configurations of HLAs, there are three broad groups of HLAs: HLA-A, HLA-B, and HLA-DR. Each set of three is called a haplotype. Every person has two specific HLAs from each of the three groups, for a total of two haplotypes (six HLAs). Each parent passes one haplotype to each child. Tissue matching for organ transplantation compares the donor's six HLAs with the recipient's six HLAs. The more that match, the more likely the organ transplant will be successful. The fewer that match, the greater the risk that the recipient's immune system will attack the donor organ.

The other key factor in HLA matching is immune reactivity (ANTIBODY reaction). It is possible to develop antibodies to HLAs that, even with a match, make it almost certain that the recipient will reject the organ. The most common cause for HLA antibodies is exposure to nonself HLA as a result of BLOOD TRANSFUSION. HLA matching is not a

component of blood typing. It is possible to have immune reactivity to multiple HLA proteins, which increases the difficulty of locating a good match for organ transplantation. Typically transplant centers like to see a match on four or more of the HLAs. A match of three or fewer strongly suggests the recipient will reject the transplanted organ.

See also ANTIBODY-MEDIATED IMMUNITY; ANTIGEN; GENOTYPE; INHERITANCE PATTERN; PHENOTYPE.

humoral immunity See ANTIBODY-MEDIATED IMMUNITY.

hypersensitivity reaction A symptomatic interaction between antibodies and allergens that causes an exaggerated and harmful response in the body, commonly called an allergic reaction. Hypersensitivity reactions range from mild to life threatening in severity and symptoms.

ANAPHYLAXIS, the most severe hypersensitivity reaction, is a life-threatening emergency that requires immediate medical attention.

There are four types of hypersensitivity reaction, classified according to the way in which the ALLERGEN or ANTIGEN activates the reaction. The classic allergic reaction is the type I hypersensitivity reaction, with exposure to an external substance (the allergen) initiating the IMMUNE RESPONSE. Types II, III, and IV hypersensitivity reactions are endogenous (within the body) responsible for IMMUNE DISORDERS (other than due to IMMUNODEFICIENCY) and AUTOIMMUNE DISORDERS.

Type I Hypersensitivity Reaction: IgE Antibody Reaction

IMMUNOGLOBULIN E (IgE), the foundation lipoprotein for ANTIBODY formation, mediates type I hypersensitivity reactions. With exposure to an external allergen, the immune response floods the BLOOD circulation with antibodies. Mast cells, basophils, and eosinophils (white blood cells that have specialized immune functions) participate in type I hypersensitivity reactions. Mast cells release HISTAMINE, PROSTAGLANDINS, and other biochemicals that set in motion interactions among various proteins and cells that guide further immune activity.

Symptoms generally occur within 15 to 30 minutes of exposure, though sometimes can emerge 10 to 12 hours after exposure. Anaphylaxis (also called anaphylactic shock) is the most severe type I hypersensitivity and is life threatening. ALLERGIC RHINITIS, ALLERGIC CONJUNCTIVITIS, ALLERGIC ASTHMA, ATOPY, and FOOD ALLERGIES are type I hypersensitivity reactions. Type I hypersensitivity reactions tend to run in families, causing researchers to suspect genetic underpinnings for the allergies.

A type I hypersensitivity reaction occurs in two stages: the induction stage, the first exposure during which the IMMUNE SYSTEM produces antibodies for the particular antigen or allergen, and the elicitation stage, during which the immune response activates the antibodies to attack the antigen or allergen. There are no symptoms during the induction stage. Each subsequent exposure to the antigen or allergen triggers the elicitation stage, resulting in symptoms. The elicitation stage lasts as long as there is allergen–antibody interaction, though symptoms may continue for some time (hours to days) afterward.

Regardless of what form symptoms take (SKIN RASH, tingling around the MOUTH, DIARRHEA), a type I hypersensitivity reaction is a systemic response—it affects and involves the body as a whole. Sensitization to an allergen is long term or lifelong because the antibody-bearing PLASMA cells (B-cell lymphocytes that specialize to produce antibodies) circulate indefinitely in the blood.

Type II Hypersensitivity Reaction: Cytotoxic Reaction

Immunoglobulin G (IgG) and immunoglobulin M (IgM) mediate cytotoxic reactions, also called antibody-mediated hypersensitivity reactions. Type II reactions occur as a result of interactions between antibodies and antigens on cell membrane surfaces. The immune response activates the COMPLEMENT CASCADE, which results in the release of biochemicals that kill the antigen-bearing cells. T-cell lymphocytes and natural killer (NK) cells also participate. Symptoms of a type II hypersensitivity reaction typically emerge within a few minutes to several hours after antibody–antigen binding.

Hemolytic ANEMIA, BLOOD TRANSFUSION reactions, Rhesus (Rh) blood reactions (erythroblastosis fetalis), PEMPHIGUS, GOODPASTURE'S SYNDROME, and many DRUG allergies (notably penicillin) are type II hypersensitivity reactions.

Type III Hypersensitivity Reaction: Immune Complex (IC) Reaction

IgG and IgM also mediate type III hypersensitivity reactions, though through different mechanisms from those that occur in type II hypersensitivity reactions. Type III hypersensitivity reactions occur when unattached antigens enter the blood circulation and activate an immune response that results in the formation of an immune complex, a conglomeration of immune proteins (immunoglobulins), platelets, neutrophils, and immune-related substances that surround the antigens. Eventually these clumps fall out of the blood circulation and settle into tissues. Type III antibodies are autoantibodies—that is, antibodies that target the body's own antigens.

Researchers do not know what precipitates the immune response in most type III reactions, though viruses such as HEPATIS A, serum sickness, and drug reactions are sometimes accountable. Symptoms develop 3 to 10 hours after the immune complex forms. ASPERGILLOSIS, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), GLOMERULONEPHRITIS, polyarteritis and other forms of VASCULITIS, and RHEUMATOID ARTHRITIS are type III hypersensitivity reactions.

Type IV Hypersensitivity Reaction: Delayed Reaction

T-cell lymphocytes (primarily helper T-cells) mediate type IV hypersensitivity reactions, also called delayed-type hypersensitivity (DTH) or cell-mediated hypersensitivity reactions. Type IV reactions take days to weeks to manifest. The rash of poison ivy, poison oak, and poison sumac represents a type IV hypersensitivity reaction. GRANULOMA is also a typical type IV hypersensitivity reaction, often to BACTERIA or fungi the body is unable to completely eliminate. Common therapeutic applications of a type IV hypersensitivity reaction include the tuberculin skin test to detect the presence of *Mycobacterium tuberculosis* and skin patch ALLERGY TESTING.

Symptoms and Diagnostic Path

Symptoms vary with the type and severity of the hypersensitivity reaction. Itching and skin rash or URTICARIA (hives) are common with type I hypersensitivity reactions. Symptoms may involve the airways (allergic asthma) or gastrointestinal tract (food allergies). Contact reactions typically involve the surface of the skin though may also produce widespread systemic symptoms. The diagnostic path may include blood tests to assess the types and levels of blood cells present in the circulation as well as to detect the types and quantities of immunoglobulins. Allergy testing can help isolate the specific allergens for type I hypersensitivity reactions. The doctor may conduct further diag-

HYPERSENSITIVITY REACTION TYPES AND SYMPTOMS

Type of Reaction	Symptoms	Typical Onset from Exposure
type I (IgE antibodies)	URTICARIA (hives), SKIN RASH, wheezing itching	15 to 30 minutes
type II (cytotoxic)	redness and swelling due to cell or tissue death	minutes to several hours
type III (immune complex)	redness and swelling (erythema and edema) pain	3 to 10 hours
type IV (cell mediated)	redness and hardness (erythema and induration) PAIN	48 to 72 hours (nongranuloma) 3 to 4 weeks (granuloma)

nostic testing to rule out other possible causes of the symptoms.

Treatment Options and Outlook

Antihistamine medications are the most effective intervention early in the onset of a type I hypersensitivity reaction, the classic allergic reaction. These medications block histamine receptors on cell membrane surfaces, effectively breaking the chain reaction effect of the immune response. The longer the hypersensitivity reaction has been under way, the less effective antihistamine medications are because the reaction moves beyond histamine release and binding. Treatment for anaphylactic symptoms is injection with EPINEPHRINE, a potent NEUROTRANSMITTER and HORMONE that effectively halts the immune response. Doctors reserve epinephrine for life-threatening hypersensitivity reactions because the drug has numerous and significant effects on cardiovascular and pulmonary function.

CORTICOSTEROID MEDICATIONS are effective for severe type I reactions and type II, III, and IV reactions. Other IMMUNOSUPPRESSIVE MEDICATIONS such as methotrexate and cyclosporine act through different mechanisms to interrupt the immune response. DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS) use various mechanisms to achieve similar results. MONOCLONAL ANTIBODIES (MABS) are showing great promise for treating hypersensitivity reactions in some people. The appropriate treatment selections depend on the type and severity of the hypersensitivity reaction and any other health conditions the person may also have.

TREATMENT OPTIONS FOR HYPERSENSITIVITY REACTION

Treatments	Effects	Effective for Type of Reaction
ANTIHISTAMINE MEDICATIONS	block HISTAMINE binding	type I
CORTICOSTEROID MEDICATIONS	suppress COMPLEMENT CASCADE, ANTIBODY activation, and eosinophil production suppress mast cell release of histamine, LEUKOTRIENES, and PROSTAGLANDINS	type II, type III, type IV type I when severe or nonresponsive to other treatment
DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS)	suppress various immune response pathways	type III
EPINEPHRINE injection	stop the immune response	type I when severe or anaphylactic
immunosuppressive agents other than corticosteroids	suppress various immune response pathways	type III and type IV
leukotriene receptor antagonist medications	block leukotriene binding	type I when ASTHMA present
MAST CELL stabilizers	prevent degranulation within mast cells to block the release of histamine, leukotrienes, and prostaglandins	type I when asthma present
MONOCLONAL ANTIBODIES (MABS)	block antibody–ANTIGEN binding	type I when asthma present type III and type IV
NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)	block the actions of prostaglandins	type III

Risk Factors and Preventive Measures

The sole risk for hypersensitivity reaction (types I, II, and III) is exposure to an allergen; the most effective prevention is avoiding such exposure. This approach is often easier said than done, especially when the allergen is an ubiquitous substance such as pollen or mold. Doctors often recommend taking antihistamine medications on a regular schedule during times when pollen counts are high to reduce hypersensitivity reactions among people who have seasonal allergies. Desensitization effectively reduces or prevents hypersensitivity reactions to specific allergens for many people, providing permanent relief.

See also ALLERGIC DERMATITIS; ALLERGY; B-CELL LYMPHOCYTE; GRANULOCYTE; LEUKOCYTE; LIVING WITH ALLERGIES; LYMPHOCYTE; MAST CELL; NATURAL KILLER (NK) CELL; T-CELL LYMPHOCYTE.

I

immune disorders Chronic conditions of the IMMUNE SYSTEM that affect the IMMUNE RESPONSE and the body's ability to protect and defend itself against INFECTION. Immune disorders generally result from a deficiency or absence of some component or structure of immune function. Such a deficiency may be primary, which is congenital (present at birth), genetic (inherited), or acquired (develops during life). People who have had their spleen surgically removed (SPLENECTOMY) also have reduced immune response, which results in increased susceptibility to infection.

IMMUNE DISORDERS

AUTOIMMUNE DISORDERS	COMMON VARIABLE IMMUNE DEFICIENCY (CVID)
HIV/AIDS	IMMUNOGLOBULIN A (IgA) deficiency
HYPERSENSITIVITY REACTION	IgM deficiency
IgA NEPHROPATHY	SEVERE COMBINED IMMUNODEFICIENCY (SCID)
IgE deficiency	Wegener's granulomatosis
PARTIAL COMBINED IMMUNODEFICIENCY (PCID)	
TOXIC EPIDERMAL NECROLYSIS	

Frequent or chronic infection is the primary symptom of an immune disorder other than HYPERSENSITIVITY REACTION (allergy). BLOOD tests for immunoglobulins and antibodies generally can diagnose immune disorders. Hypersensitivity reactions generate symptoms according to the type of reaction and may include symptoms of ALLERGIC RHINITIS, ALLERGIC CONJUNCTIVITIS, ALLERGIC DERMATITIS, or ALLERGIC ASTHMA. ALLERGY TESTING is the preferred diagnostic approach for identifying the allergens responsible for hypersensitivity reaction, though often a person knows the cause of an allergy.

Immune disorders are generally chronic, which means treatment can improve symptoms but not cure or end the condition. Common medication therapies for immune disorders include ANTIHISTAMINE MEDICATIONS, NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), CORTICOSTEROID MEDICATIONS, leukotriene receptor antagonists, MAST CELL stabilizers, and DISEASE-MODIFYING RHEUMATOID DRUGS (DMARDS). The particular medication regimen depends on the immune disorder and the individual's symptoms.

See also ANTIBODY; ATOPY; GENETIC DISORDERS; IMMUNITY; IMMUNOCOMPROMISED; IMMUNODEFICIENCY; LEUKOTRIENES; LIVING WITH IMMUNE DISORDERS.

immune response The multiple mechanisms and processes through which the body identifies and reacts to antigens. The immune response is the body's primary means of protecting itself from INFECTION. There are three independent yet complementary immune response pathways: ANTIBODY-MEDIATED IMMUNITY (also called humoral immunity), CELL-MEDIATED IMMUNITY, and the COMPLEMENT CASCADE. As well, the immune response stimulates activity from the NERVOUS SYSTEM and the endocrine system.

The immune response relies largely on ANTIBODY–ANTIGEN binding. Antigens are molecules that identify cells to the IMMUNE SYSTEM. Antibodies are molecules the immune system produces to bind with nonself antigens—antigens on cells that do not belong to the body. With antibody–antigen binding, the antibody releases proteins called opsonins that mark the antigen-bearing cell for destruction by killer T-cells and natural killer (NK) cells. Monocytes (in the BLOOD circulation) and macrophages (in the tissues) consume the cellular debris remaining after the marked cell's destruction. Antibody–antigen binding also activates the complement cascade, a biochemical response that

produces proteins that attach to and damage the cell membrane of cells that the immune response identifies as nonself.

A key feature of the immune response is INFLAMMATION, the process by which the body increases the ability of PLASMA, the liquid component of blood, to seep into the tissues (interstitial spaces). HISTAMINE and PROSTAGLANDINS are the primary agents of the inflammatory response. Inflammation floods the tissues with immune molecules to extend the immune response beyond the blood and the LYMPH. Inflammation also serves to contain the infection, keeping it from spreading beyond its point of origin to other areas of the body.

For further discussion of the immune response within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ALLERGEN; ECHINACEA; GOLDENSEAL; HUMAN LEUKOCYTE ANTIGENS (HLAS); HYPERSENSITIVITY REACTION; MACROPHAGE; MAJOR HISTOCOMPATIBILITY COMPLEX (MHC); MAST CELL; MONOCYTE; NATURAL KILLER (NK) CELLS; PHAGOCYTOSIS.

immune system The structures, substances, and processes that protect the body from INFECTION. These include organs, tissues, cells, and molecules. The immune system functions in close collaboration with the NERVOUS SYSTEM and the endocrine system.

The main organs and tissues of the immune system include

- BONE MARROW
- THYMUS
- SPLEEN
- lymph nodes
- BLOOD
- LYMPH
- adenoids and tonsils
- APPENDIX
- MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT)
- SKIN
- tears
- saliva

The primary cells of the immune system include

- B-cell lymphocytes (PLASMA cells, memory B-cells)
- T-cell lymphocytes (helper T-cells, cytotoxic T-cells, memory T-cells, suppressor T-cells)
- granulocytes (neutrophils, eosinophils, and basophils)
- macrophages and dendritic cells
- mast cells
- monocytes
- M cells
- natural killer (NK) cells

Key molecules of the immune system include

- HUMAN LEUKOCYTE ANTIGENS (HLAS)
- complement factors
- CLUSTERS OF DIFFERENTIATION
- IMMUNOGLOBIN
- antigens
- antibodies
- PROSTAGLANDINS
- HISTAMINE
- LEUKOTRIENES
- CYTOKINES (CHEMOKINES, INTERLEUKINS, MONOKINES, INTERFERONS, LYMPHOKINES, COLONY-STIMULATING FACTORS [CSFS], and TUMOR NECROSIS FACTORS [TNFS])

For further discussion of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; ANTIGEN; ANTIBODY-MEDIATED IMMUNITY; B-CELL LYMPHOCYTE; CELL-MEDIATED IMMUNITY; COMPLEMENT CASCADE; GRANULOCYTE; IMMUNE RESPONSE; LYMPH NODE; LYMPHOCYTE; MACROPHAGE; MAJOR HISTOCOMPATIBILITY COMPLEX (MHC); MONOCYTE; NATURAL KILLER (NK) CELL; PSYCHONEUROIMMUNOLOGY; T-CELL LYMPHOCYTE.

immunity An established base of protection against INFECTION. Immunity may be innate, pas-

sive, or acquired. INNATE IMMUNITY, also called natural immunity, is present at birth and provides effective protection against a broad base of common pathogens. Innate immunity is limited in scope. PASSIVE IMMUNITY is ANTIBODY-specific but present without activation of the IMMUNE RESPONSE. A newborn has passive immunity based on the antibodies present in his or her mother's BLOOD. BLOOD TRANSFUSION, PLASMA transfusion, and administration of GAMMAGLOBULIN also convey passive immunity to the recipient. Passive immunity is short term. The body develops acquired immunity through exposure to antigens via infection or vaccination. Acquired immunity is ANTIGEN-specific and long term, often lifelong.

For further discussion of immunity within the context of the structures and functions of the IMMUNE SYSTEM, please see the overview section "The Immune System and Allergies."

See also ANTIBODY-MEDIATED IMMUNITY; CELL-MEDIATED IMMUNITY; PATHOGEN; VACCINE.

immunoablation The therapeutic destruction of the body's IMMUNE RESPONSE, typically to prepare for BONE MARROW TRANSPLANTATION or STEM CELL transplantation. Immunoablation is usually a step in the treatment process for certain cancers and AUTOIMMUNE DISORDERS, such as severe MULTIPLE SCLEROSIS. High-DOSE CHEMOTHERAPY and RADIATION THERAPY are the most common methods of immunoablation. The goal is to remove all T-cell lymphocytes from the BLOOD, which destroys the body's CELL-MEDIATED IMMUNITY. Until the person's IMMUNE SYSTEM restores immune functions, the person is extremely vulnerable to any INFECTION. A person who has undergone immunoablation stays in a hospital in strict isolation until immune function returns after bone marrow or stem cell transplantation.

See also CANCER TREATMENT OPTIONS AND DECISIONS; LEUKEMIA; MULTIPLE MYELOMA; T-CELL LYMPHOCYTE.

immunocompromised Any circumstance in which the IMMUNE SYSTEM lacks the capacity, as the consequence of an acquired health condition or a medication SIDE EFFECT, to protect the body from INFECTION. DIABETES is the most common reason people become immunocompromised. People who are taking IMMUNOSUPPRESSIVE THERAPY after ORGAN TRANSPLANTATION or to treat severe AUTOIMMUNE DISORDERS are also immunocompromised. People who are immunocompromised often struggle to fight off common infections such as COLDS and URINARY TRACT INFECTION (UTI) and are vulnerable to OPPORTUNISTIC INFECTION (an infection that a healthy immune system would easily rebuff).

See also ANTIBIOTIC PROPHYLAXIS; IMMUNE DISORDERS; LIVING WITH IMMUNE DISORDERS.

immunodeficiency The absence of IMMUNE SYSTEM components essential for proper IMMUNE RESPONSE and protection from INFECTION. Immunodeficiency may be congenital (present at birth) or acquired (develop later in childhood or adulthood). As well, immunodeficiency is a consequence of therapies intended to compromise immune function, such as RADIATION THERAPY, CHEMOTHERAPY, and IMMUNOSUPPRESSIVE THERAPY.

Congenital immunodeficiency is genetic (the result of a GENE MUTATION) and may be inherited. Inherited immunodeficiencies can include IMMUNOGLOBULIN deficiencies, disorders of B-cell lymphocytes, disorders of T-cell lymphocytes, and complement disorders. A child born without a THYMUS or a SPLEEN will have multiple immunodeficiencies because these structures are crucial for LEUKOCYTE (white BLOOD cell) formation and maturation.

Acquired immunodeficiency generally occurs as a result of infections, AUTOIMMUNE DISORDERS, or severe trauma (such as BURNS) that challenges the immune system's capabilities. Conditions such as DIABETES and CYTOMEGALOVIRUS (CMV) infection commonly cause immunodeficiency. The HIV/AIDS infection is one of the most serious acquired immunodeficiencies, as it eventually destroys the immune system.

Immunodeficiency disorders are not currently preventable or curable; diligent treatment can usually keep disease progression and symptoms in check. Treatment for immunodeficiency disorders depends on the cause of the disorder and the symptoms it creates. Medications and IMMUNOTHERAPY (biologic response modification) allow many people who have immunodeficiency disorders live fairly normal lifestyles.

See also ANTIBODY-MEDIATED IMMUNITY; B-CELL LYMPHOCYTE; CELL-MEDIATED IMMUNITY; COMMON VARI-

ABLE IMMUNODEFICIENCY (CVID); COMPLEMENT CASCADE; IMMUNE DISORDERS; LIVING WITH IMMUNE DISORDERS; PARTIAL COMBINED IMMUNODEFICIENCY (PCID); SEVERE COMBINED IMMUNODEFICIENCY (SCID); T-CELL LYMPHOCYTE.

immunoglobulin A protein structure the IMMUNE SYSTEM produces. Immunoglobulins are the foundation molecules for the formation of antibodies. Immunoglobulins circulate in the BLOOD. The immunoglobulin's class designation reflects its molecular structure, which in turn dictates the action of the immunoglobulin. The five major classes of immunoglobulin provide different kinds of antibodies:

- Immunoglobulin A (IgA) is the main immunoglobulin in the body's secretions (tears, saliva, and mucus) and in colostrum, the first discharge from the mother's breasts after childbirth. It is the second most abundant immunoglobulin in the blood circulation. IgA boosts the IMMUNE RESPONSE capacity of the various MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) structures. IgA blood levels decrease in lymphoblastic leukemias and increase in certain AUTOIMMUNE DISORDERS, notably RHEUMATOID ARTHRITIS and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).
- Immunoglobulin D (IgD) resides on the surface of the cell membrane of B-cell lymphocytes. Its primary role is to bind with antigens. IgD blood levels increase with chronic infections and certain myelomas.
- Immunoglobulin E (IgE) produces the antibodies responsible for HYPERSENSITIVITY REACTION as well as primary INFECTION-fighting antibodies. It also is the immune response's main defense against parasitic infection. IgE is the least abundant of the immunoglobulins in the blood circulation. Blood levels of IgE rise with hypersensitivity reactions.
- Immunoglobulin G (IgG) is the most abundant and versatile of the immunoglobulins. It makes up 75 percent of the immunoglobulin in the blood circulation. IgG binds with many types of leukocytes and activates the COMPLEMENT CASCADE. IgG is the only immunoglobulin that can cross the placental barrier between mother and fetus. IgG blood levels increase with infection and rheumatoid arthritis and decreases with lymphoblastic LEUKEMIA.
- Immunoglobulin M (IgM) is the third most abundant class of immunoglobulin in the blood circulation. The first contact with an ANTIGEN causes a B-CELL LYMPHOCYTE to produce IgM. IgM antibodies help collect cellular debris for more efficient PHAGOCYTOSIS. Blood levels of IgM increase with infectious mononucleosis, MALARIA, SLE, and rheumatoid arthritis.

Immunoglobulins collected from donated blood and PLASMA are blended to produce GAMMAGLOBULIN, a therapeutic form that boosts the nonspecific immune response.

For further discussion of immunoglobulins within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; ANTIBODY-MEDIATED IMMUNITY; LEUKOCYTE; LYMPHOCYTE; MONONUCLEOSIS, INFECTIOUS; VACCINE.

immunosenescence A decline in immune function and IMMUNE RESPONSE that occurs with aging. Researchers believe immunosenescence accounts for the increase in cancer and infections such as INFLUENZA and PNEUMONIA in people of old age. The decline occurs in both CELL-MEDIATED IMMUNITY (sometimes called cytotoxic immunity), in which T-cell lymphocytes attack and kill foreign antigens, and humoral immunity, in which B-cell lymphocytes generate the antibodies that circulate in the BLOOD. Though immunosenescence appears a normal physiologic process in that it happens to everyone as they grow older, researchers question whether it is an intrinsic function under genetic regulation or an extrinsic reaction to environmental factors, ranging from EATING HABITS to toxic exposure.

See also AGING, EFFECTS ON IMMUNE RESPONSE; ANTIBODY; ANTIGEN; APOPTOSIS; B-CELL LYMPHOCYTE; CELL STRUCTURE AND FUNCTION; LYMPHOCYTE; T-CELL LYMPHOCYTE.

immunosuppressive medications Drugs that limit or suppress some aspect of the IMMUNE RESPONSE. Immunosuppressive medications such as cyclosporine work by many different mechanisms

with the goal being to block the body's rejection of a transplanted organ or bone marrow and to prevent GRAFT VS. HOST DISEASE. Common immunosuppressive medications include

- CORTICOSTEROID MEDICATIONS, which inhibit the production of eosinophils, suppress the COMPLEMENT CASCADE, and block the activation of antibodies
- DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS), which block the immune response in such of a way as to alter, at least temporarily, the course of the disease
- cytotoxic agents, which kill cells (cells that replicate rapidly, such as BLOOD cells, are more greatly affected)

Doctors prescribe immunosuppressive medications to treat AUTOIMMUNE DISORDERS, HYPERSENSITIVITY REACTION, and to prevent an immune response that targets a transplanted organ. Often doctors prescribe these medications in combination to quell the immune response on several fronts. This allows lower dosages for each type of medication, reducing the overall amount of medication the person must take and minimizing side effects. The approach also provides greater relief in severe presentations of chronic inflammatory diseases such as RHEUMATOID ARTHRITIS and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).

Immunosuppressive medications have numerous side effects, DRUG interactions, and risks specific to the medication. In general, the primary risk of immunosuppressive medications is INFECTION, particularly OPPORTUNISTIC INFECTION. Though doctors try to maintain a balance of immune suppression that controls symptoms yet allows the body to protect itself from infection, IMMUNOSUPPRESSIVE THERAPY opens the gateway for pathogens to invade. Aggressive antibiotic therapy then becomes necessary to eradicate the infection.

See also ANTIBIOTIC MEDICATIONS; ANTIHISTAMINE MEDICATIONS; CHEMOTHERAPY; DRUG INTERACTION; LIVING WITH IMMUNE DISORDERS; ORGAN TRANSPLANTATION; PATHOGEN.

immunosuppressive therapy Treatments that limit or suppress the IMMUNE RESPONSE. Such treatment may incorporate IMMUNOSUPPRESSIVE MEDICATIONS such as CORTICOSTEROID MEDICATIONS, DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS), CHEMOTHERAPY, RADIATION THERAPY, and MONOCLONAL ANTIBODIES (MABS).

Doctors may prescribe short-term immunosuppressive therapy (two to six weeks) to treat moderate to severe type I HYPERSENSITIVITY REACTION or to reduce INFLAMMATION due to injury. Long-term immunosuppressive therapy is generally a treatment option for chronic AUTOIMMUNE DISORDERS such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) and RHEUMATOID ARTHRITIS. People who have had organ transplants must take lifelong immunosuppressive therapy to reduce the risk for organ rejection and GRAFT VS. HOST DISEASE. The risk for complications and side effects rises the longer a person is on immunosuppressive therapy.

Immunoablation (the administration of high-DOSE chemotherapy or radiation therapy) wipes out the immune response altogether by killing the BONE MARROW, which removes all leukocytes and their subtypes from the IMMUNE SYSTEM's resource arsenal. This form of immunosuppressive therapy prepares the body to receive BONE MARROW TRANSPLANTATION or STEM CELL transplantation, which then rebuilds the immune system from the marrow up.

See also COMPLEMENT CASCADE; LEUKOCYTE; LIVING WITH IMMUNE DISORDERS; ORGAN TRANSPLANTATION; PROSTAGLANDINS.

immunotherapy The therapeutic use of biologic agents to manipulate the mechanisms of the IMMUNE SYSTEM. Immunotherapy, also called biologic response modification, is an effective method for reducing INFLAMMATION and other aspects of the IMMUNE RESPONSE to treat inflammatory AUTOIMMUNE DISORDERS such as RHEUMATOID ARTHRITIS. Immunotherapy is also a treatment option for many forms of cancer. The common types of immunotherapy are

- CYTOKINES such as INTERLEUKINS and INTERFERONS, which boost the cytotoxic (cell-killing) actions of T-cell lymphocytes and natural killer (NK) cells
- COLONY-STIMULATING FACTORS (CSFS), which stimulate the growth of leukocytes and lymphocytes (white BLOOD cells) in the BONE MARROW

- MONOCLONAL ANTIBODIES (MABS), which stimulate specific ANTIBODY activity

Vaccines are among the most effective and basic forms of immunotherapy. A VACCINE introduces a substance such as a VIRUS or strain of BACTERIA into the body at a level significant enough to stimulate an immune response yet mild enough to avoid establishing INFECTION in most people. Researchers are now exploring ways to apply the principles of vaccines to cancer treatment and CANCER PREVENTION. CANCER VACCINES, currently in investigational studies, attempt to modify the immune response by creating antibodies that will recognize the antigens on cancer cells should the cancer recur after initial treatment.

See also CANCER TREATMENT OPTIONS AND DECISIONS; GENE THERAPY; LEUKOCYTE; LYMPHOCYTE; NATURAL KILLER (NK) CELL; T-CELL LYMPHOCYTE; VACCINE.

inflammation The release of fluid (PLASMA) from the BLOOD vessels into the tissues, facilitating the movement of key immune proteins and other molecules to the site of injury or INFECTION. Inflammation is the mechanism of the IMMUNE RESPONSE for containing and mitigating whatever damage has occurred. PROSTAGLANDINS, which mast cells release, are the primary instigators of the inflammatory response. Inflammation occurs as a coupling of increased blood circulation to the area with increased capillary permeability (the amount of fluid the capillaries allow to escape into the spaces between cells). Though inflammation accompanies infection, it does not always indicate that an infective process is under way.

Plasma, the liquid portion of the blood, contains numerous immune elements, including antibodies, CYTOKINES, and complement factors. Swelling, which is the hallmark of inflammation, indicates that this mechanism is succeeding in getting the necessary immune elements to the site. IMMUNOGLOBULIN E (IgE) and certain of the cytokines are instrumental in the inflammation process. Inflammation typically causes swelling, PAIN, FEVER, and often redness of the SKIN at the site of the inflammation. When joints are inflamed, as in RHEUMATOID ARTHRITIS, the JOINT often feels stiff and has limited range of motion. TENDONITIS and BURSITIS are also common presentations of inflammation.

Treatment for inflammation is often NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS), or CORTICOSTEROID MEDICATIONS, depending on the cause. When appropriate, ice to the local area provides relief from pain and helps contract the blood vessels to slow the flow of blood. The latter, in turn, reduces the amount of fluid that enters the tissues. Reducing use of the affected area facilitates HEALING and the body's reabsorption of the excess interstitial fluid, though movement to keep the joints from stiffening is also important. PHYSICAL THERAPY, TAI CHI, YOGA, and MASSAGE THERAPY are among the methods that help maintain mobility and FLEXIBILITY. Treatment also targets the circumstance causing the inflammation whenever possible, such as any underlying injury or condition.

For further discussion of inflammation within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANALGESIC MEDICATIONS; ANTIBODY; ANTIGEN; COMPLEMENT CASCADE; MAST CELL.

innate immunity The level of immune protection with which an individual is born. Researchers believe innate immunity, also called natural immunity, is the result of genetically encoded PATHOGEN recognition—that is, GENE-regulated ability to identify and mount an IMMUNE RESPONSE to neutralize certain BACTERIA, viruses, and other substances capable of causing INFECTION or otherwise doing harm to the body. The immune cell receptors recognize key characteristics of molecular structure common to many pathogens, called pathogen-associated molecular patterns (PAMPs), rather than specific pathogens. Their response does not require prior exposure before activation; thus PAMPs respond immediately to the presence of pathogens that fit the pattern. Innate immunity is species specific, which is why most infections cannot pass from one species to another. Pathogens capable of infecting multiple species are those that mutate for each species.

For further discussion of immunity within the context of the structures and functions of the

immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY-MEDIATED IMMUNITY; CELL-MEDIATED IMMUNITY; VIRUS.

interferons CYTOKINES (molecules on the surface of cell membranes that direct cell activity) that block the activity of viruses and mediate numerous aspects of the IMMUNE RESPONSE. There are more than a dozen type 1 INTERFERONS, the most abundant of which are interferon-alpha and interferon-beta. B-cell lymphocytes and T-cell lymphocytes produce type 1 interferons, which primarily direct the functions of macrophages and natural killer (NK) cells in responding to viruses. Activated T-cells produce interferon-gamma, which is the only type 2 interferon. Interferon-gamma helps regulate INFLAMMATION.

Interferon-alpha and interferon-beta have strong tumor-suppression actions, which has led to their therapeutic use for certain kinds of cancer. Oncologists (doctors who specialize in treating cancer) administer recombinant forms of interferons (interferons that are synthesized in a laboratory using RECOMBINANT DNA technology) by injection to treat chronic myeloid LEUKEMIA, hairy cell leukemia, malignant melanoma, and some types of lymphoma. Doctors also use therapeutic interferons to treat HEPATITIS C and MULTIPLE SCLEROSIS. Pegylated interferons are synthesized to include polyethylene glycol, which delays the rate at which the body absorbs injected interferons.

See also B-CELL LYMPHOCYTE; CHEMOKINES; INTERLEUKINS; LYMPHOCYTE; LYMPHOKINES; MACROPHAGE; NATURAL KILLER (NK) CELL; T-CELL LYMPHOCYTE; VIRUS.

interleukins CYTOKINES that influence the growth, proliferation, and activity of leukocytes and other BLOOD cells. Leukocytes produce interleukins. There are 12 major interleukins, identified as interleukin 1 (IL-1) through IL-12. Among those significant to LEUKOCYTE development are

- IL-3, which influences blood stem cell differentiation into the various types of blood cells; leukocyte differentiation into granulocytes, monocytes, and lymphocytes; GRANULOCYTE differentiation into basophils; and LYMPHOCYTE differentiation into B-cell lymphocytes and T-cell lymphocytes
- IL-5, which influences leukocyte differentiation into eosinophils
- IL-7, which stimulates the BONE MARROW to produce lymphocytes

The interleukins also regulate the actions of leukocytes—monocytes, neutrophils, basophils, macrophages, B-cell lymphocytes, T-cell lymphocytes, natural killer (NK) cells, mast cells, PLASMA cells—in the IMMUNE RESPONSE, notably the INFLAMMATION process. The role of interleukins in the production and activity of basophils and neutrophils, the cells of the immune response largely responsible for inflammation, has come under scrutiny as a key factor in the development of conditions such as ATHEROSCLEROSIS. Research is under way to investigate methods to manipulate interleukin production and levels to reduce the inflammatory response in such circumstances, thus diminishing or eliminating the disease process. Other research is investigating therapeutic administration of interleukins to treat HIV/AIDS. Doctors currently use some synthesized interleukins therapeutically (notably IL-2) to treat certain types of cancer.

See also B-CELL LYMPHOCYTE; BLOOD STEM CELLS; INTERFERONS; LEUKOCYTE; MACROPHAGE; MAST CELL; MAJOR HISTOCOMPATIBILITY COMPLEX (MHC); MONOCYTE; NATURAL KILLER (NK) CELL; T-CELL LYMPHOCYTE.

leukotrienes Molecules that instigate INFLAMMATION during an IMMUNE RESPONSE. Mast cells secrete leukotrienes in response to stimulation by IMMUNOGLOBULIN E (IgE). Leukotrienes are derived from arachidonic acid, which is the same base source (precursor) as that of PROSTAGLANDINS, the other primary agents of inflammation. The actions of leukotrienes are most apparent in ASTHMA, in which they cause the bronchioles (tiny bronchi deep within the LUNGS) to constrict. Leukotriene release becomes more rapid with each HYPERSENSITIVITY REACTION. Leukotrienes also attract eosinophils, which cause swelling in the bronchial mucosa (mucous membrane lining of the bronchi). In inflammatory responses outside the pulmonary system, leukotrienes attract neutrophils with similar effect (swelling and discomfort). Eosinophils and neutrophils are types of granulocytes.

See also GRANULOCYTE; HISTAMINE; MAST CELL.

living with allergies About 50 million Americans live with allergies—to pollens, animal danders, latex, fragrances, foods, drugs, and other substances—that cause them to alter their lifestyles. Most people can reduce exposure to allergens enough to lessen symptoms.

Outdoor Allergens

The primary outdoor allergens are pollens and molds. Pollen is the powdery and often microscopic granules that are the male cells of plants. The plant disperses pollen into the air, which carries it to other plants. The dusting of pollen on plants of the same species fertilizes them, permitting them to propagate. The pollens most likely to cause a HYPERSENSITIVITY REACTION are grasses and trees. Tree pollens are highest in early spring and grass pollens (including weeds) are highest in early summer. Both tree and grass pollens remain high through summer and into early autumn in most regions of the United States. Molds are also microscopic, airborne substances, though correlate to weather conditions rather than seasons. Molds are highest when the weather is cool and wet. Raking leaves in the autumn is a major risk for exposure to molds.

Many weather reports include local pollen counts and mold counts. Counts that are moderate to high are likely to cause ALLERGY symptoms in people who are allergic; very high counts may cause symptoms in people who do not typically have seasonal allergies. Because pollens and molds are airborne, it is difficult to escape them. Allergists recommend ANTIHISTAMINE MEDICATIONS or DESENSITIZATION to mitigate symptoms. Staying indoors is not usually an effective or practical strategy.

Steps that may help include taking off outdoor clothing immediately upon coming indoors and washing the face, arms, hands, and other exposed areas with soap and water (showering is best). Washing the hands especially helps limit spreading pollen to the NOSE and EYE via contact. Some people can reduce their symptoms by wearing a mask over the face and nose during outdoor activities when pollen and mold counts are high. As well, pollen counts are highest in the early morning. Central air-conditioning in the home and in the car helps filter pollens and other particulates.

Being outdoors brings the risk of exposure to other allergens as well. People who are allergic to the sting of bees and wasps have a high risk of exposure during spring and summer when plants are in bloom. Wasps and related stinging insects become active in the autumn, especially in

wooded areas or areas where there is mud. Contact with poison ivy, poison oak, or poison sumac can cause symptoms any time of the year, though this is more of a problem in spring and summer.

Indoor Allergens

Indoor allergens are commonly dust, insect droppings, and pet dander. Cockroach droppings are the prime cause of ALLERGIC ASTHMA in urban areas, especially in children. Cockroaches are attracted to moisture and food debris; keeping living areas dry and clean reduces the attraction. Dust mite droppings are also a significant cause of allergic ASTHMA and ALLERGIC RHINITIS. Dust mites also prefer humid environments, though their food source is the microscopic flakes of SKIN that people continually shed. These flakes accumulate in bedclothes and bed linens especially. Keeping the bedroom dry and washing sheets once a week in hot water helps reduce the dust mite population.

About 80 percent of American households have pets. About the same percentage of people who have allergies are allergic to pet dander (most often cat dander). Some studies have found animal dander is as pervasive in the indoor environment as is pollen in the outdoor environment. Desensitization is the recommendation of most allergists for people who are allergic but want to have pets. Though desensitization may take three to five years to become fully effective, it is a permanent solution. There are no pets that are "low allergy." The length of an animal's coat has little relationship to its ability to evoke an allergic reaction. Other measures include washing the hands and changing the clothes after handling an animal, and keeping pets out of the bedroom.

Central heating and air-conditioning are effective for controlling humidity as well as filtering the air. Central vacuum systems are also helpful because they deposit vacuumed debris outside the living area, usually into a container in the garage or basement. High-efficiency particulate air (HEPA) filters can remove many kinds of allergens from the air.

See also ALLERGEN; ALLERGY TESTING; QUALITY OF LIFE.

living with immune disorders Living with an immune disorder requires special attention to circumstances that increase the risk for INFECTION. IMMUNE DISORDERS increase susceptibility to infection either as a direct result of the disease process or, in AUTOIMMUNE DISORDERS, as a consequence of the medications necessary to keep symptoms in check. The most important factor for controlling the symptoms of immune disorders is taking medications as prescribed. Immune function is complex, and often the therapeutic approach combines different kinds of medications to achieve an overall balance to the best extent possible within the parameters of the disease process. Though many complementary approaches are beneficial, some may interfere with conventional treatments and medications.

Nutritious EATING HABITS and regular physical activity benefit the IMMUNE SYSTEM in innumerable ways. The appropriate NUTRIENTS give the body the building blocks—amino acids—it needs to make the components of the IMMUNE RESPONSE. Autoimmune conditions may restrict physical activity, yet physical activity helps maintain optimal function. PHYSICAL THERAPY and MASSAGE THERAPY are conventional means for improving range of motion, STRENGTH, and FLEXIBILITY. YOGA, TAI CHI, and qi gong are alternative approaches that can do the same, along with MEDITATION to help relieve stress and improve mental clarity and focus. BIOFEEDBACK and HYPNOSIS are other methods to manage symptoms and establish a sense of control or peaceful coexistence with the condition. Numerous studies suggest a surprisingly intricate relationship between stress, emotion, and immune function, making stress management particularly important with chronic immune dysfunction.

Efforts to prevent the chronic infections that often accompany immune disorders or the use of IMMUNOSUPPRESSIVE MEDICATIONS to treat autoimmune disorders include limiting exposure to other people who are sick (such as during cold and flu season). Frequent HAND WASHING is an effective means for containing pathogens.

See also LIVING WITH ALLERGIES; HYPERSENSITIVITY REACTION; PATHOGEN; PSYCHONEUROIMMUNOLOGY; QUALITY OF LIFE; STRESS AND STRESS MANAGEMENT.

lymphokines CYTOKINES that convey biochemical messages among lymphocytes (a type of white

BLOOD cell) to direct their actions during an IMMUNE RESPONSE. B-cell lymphocytes and T-cell lymphocytes both secrete lymphokines. Lymphokines activate and coordinate numerous immune functions across the spectrum of the immune response. They also stimulate cell growth and activation and stimulate MACROPHAGE activity.

See also B-CELL LYMPHOCYTE; COMPLEMENT CASCADE; INTERFERONS; INTERLEUKINS; LEUKOCYTE; LYMPHOCYTE; MONOKINES; T-CELL LYMPHOCYTE.

M

macrophage A MONOCYTE that leaves the BLOOD circulation and takes up residence in the tissues. Once there, the cell undergoes several changes:

- It greatly enlarges.
- It develops pseudopods (footlike projections) that permit it to move through tissue.
- It increases the amount of lysozyme its granules contain, increasing its ability to consume cellular debris.

Macrophages, the IMMUNE SYSTEM's tissue-based scavengers, are part of the MONONUCLEAR PHAGOCYTE SYSTEM. They engulf, dismantle, and consume the carcasses of cells that other immune cells destroy and of cells that die naturally (APOPTOSIS). They also absorb and breakdown the particulate debris from toxins, BACTERIA, viruses, and other substances. Macrophages also respond to the inflammatory process, contributing to INFLAMMATION and the formation of granulomas. As well, macrophages are key to ANTIGEN presentation and processing, the mechanism by which T-cell lymphocytes and B-cell lymphocytes recognize nonself antigens. As the macrophage dismantles a substance, it displays the substance's antigens, along with the relevant MAJOR HISTOCOMPATIBILITY COMPLEX (MHC), on the surface of its cell membrane for lymphocytes to detect. Lymphocytes ignore debris that belongs to the body. Debris that is foreign activates an IMMUNE RESPONSE.

For further discussion of macrophages within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also B-CELL LYMPHOCYTE; GRANULOMA; LYMPHOCYTE; NATURAL KILLER (NK) CELL; T-CELL LYMPHOCYTE; VIRUS.

major histocompatability complex (MHC) The group of genes, located on CHROMOSOME 6, that determine the HUMAN LEUKOCYTE ANTIGENS (HLAS) the body's cells carry on their cell membranes. HLAs are unique proteins that cell membranes display to identify themselves to the IMMUNE SYSTEM. There are three types of MHC:

- Class I MHC encodes the HLAs that all nucleated cells and platelets in the body carry to identify them as self cells (the body's own cells).
- Class II MHC encodes the HLAs that lymphocytes, macrophages, dendritic cells, and other substances involved in ANTIGEN processing carry. These HLAs are fundamental to ANTIBODY-MEDIATED IMMUNITY and are also responsible for GRAFT VS. HOST DISEASE and organ rejection in people who undergo ORGAN TRANSPLANTATION.
- Class III MHC encodes the immunoglobulins from which the immune system forms antibodies.

MHC is central to antigen processing. When a MACROPHAGE or dendritic cell (phagocytes, also called scavenger cells, in the MONONUCLEAR PHAGOCYTE SYSTEM) consumes cellular debris, it displays the antigens of the debris alongside its own HLA. This comparison display allows T-cell lymphocytes to recognize the cellular debris as self or nonself and respond accordingly. Self antigen evokes no reaction; nonself antigen mobilizes the IMMUNE RESPONSE.

See also ANTIBODY; CELL-MEDIATED IMMUNITY; COMPLEMENT CASCADE; GENE; IMMUNOGLOBULIN; LYMPHOCYTE; MACROPHAGE; PHAGOCYTE; PHAGOCYTOSIS; PLATELET; T-CELL LYMPHOCYTE.

mast cell A granulated LEUKOCYTE that resides in tissues throughout the body. When the IMMUNE RESPONSE stimulates mast cells, they release PROSTAGLANDINS, HISTAMINE, and other biochemicals from their granules. Mast cells are primarily responsible for the symptoms that are the hallmark of the HYPERSENSITIVITY REACTION: INFLAMMATION, itching, SKIN RASH, coughing, and sneezing. Mast cells have an abundant presence in the tissues of mucous membranes such as the NOSE, pulmonary tract (TRACHEA and bronchi), and gastrointestinal tract. Mast cells also infiltrate the connective tissues. They respond to the stimulation of complement factors and to IMMUNOGLOBULIN E (IgE) antibodies.

For further discussion of mast cells within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; COMPLEMENT CASCADE; COUGH; LIVING WITH ALLERGIES; MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); SNEEZE.

monoclonal antibodies (MAbs) Antibodies produced in a laboratory using RECOMBINANT DNA technology. MAbs derive from cloned mouse SPLEEN cells (hence the designation "monoclonal") containing the desired ANTIBODY fused with human myeloma cells. Mouse cells have proteins very similar to the proteins of human cells. Human myeloma cells, because they are cancer cells, have the ability to replicate without limitation. The myeloma cells arise from B-cell lymphocytes, which produce antibodies.

When scientists fuse the two cells together, they achieve cells (called hybridomas) that combine the desired ANTIGEN sensitization with the ability to endlessly replicate antibody-producing cells. After fusion, scientists can attach radioactive molecules for diagnostic imaging or to deliver fatal radiation to specific cells (called conjugated MAbs). Doctors then can inject MAbs into people to stimulate the IMMUNE RESPONSE as a mechanism for fighting INFLAMMATION (such as in RHEUMATOID ARTHRITIS) and certain types of cancer or to specifically target certain cells for death without affecting other cells. Indiscriminate cell death is a significant limitation of current CHEMOTHERAPY.

A key limitation of therapeutic MAbs is that the body recognizes them as nonself and configures antibodies against them. MAbs are highly effective for the first treatment, then may be less effective or initiate a HYPERSENSITIVITY REACTION in subsequent treatment efforts.

THERAPEUTIC MONOCLONAL ANTIBODIES (MABS)

abciximab (ReoPro)	alemtuzumab (MAb Campath)
bevacizumab (Avastin)	cetuximab (Erbitux)
daclizumab (Zenapax)	infliximab (Remicade)
lym-1 (Oncolym)	muromonab-CD3 (OKT3)
omalizumab (Xolair)	rituximab (Rituxan)
tositumomab (Bexxar)	trastuzumab (Herceptin)

For further discussion of MAbs within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also B-CELL LYMPHOCYTE; CANCER TREATMENT OPTIONS AND DECISIONS; IMMUNOTHERAPY; INTERFERONS; INTERLEUKINS; MOLECULARLY TARGETED THERAPIES.

monokines CYTOKINES that convey biochemical messages among monocytes (white BLOOD cells in the blood circulation) and macrophages (white blood cells that reside in the tissues). Monokines direct the actions of these immune cells during the IMMUNE RESPONSE, stimulating and coordinating numerous functions. There is some overlap between monokines and LYMPHOKINES (which lymphocytes produce).

See also COMPLEMENT CASCADE; IMMUNE SYSTEM; INTERFERONS; INTERLEUKINS; LEUKOCYTE; LYMPHOCYTE; MACROPHAGE; MONOCYTE.

mononuclear phagocyte system The combined activity of the IMMUNE SYSTEM's phagocytes—monocytes in the BLOOD circulation and macrophages in the tissues—to consume cellular debris. These cells are scavengers within the body, responsible for cleaning up after B-cell lymphocytes, T-cell lymphocytes, and natural killer (NK) cells. They also clear the debris that results from normal cell death (APOPTOSIS). They are called mononuclear because their cell structure contains a single nucleus; neutrophils, which are also phagocytes, have multiple nuclei (and are called polymorphonuclear). The COMPLEMENT CASCADE (an interaction of proteins or

factors that begins with ANTIBODY–ANTIGEN binding) is the primary alert mechanism that activates the mononuclear phagocyte system. Monocytes and macrophages work in a coordinated fashion, communicating via CYTOKINES (cell-originated biochemical messages) with other cells involved in the IMMUNE RESPONSE.

For further discussion of the mononuclear phagocyte system within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also B-CELL LYMPHOCYTE; CELL STRUCTURE AND FUNCTION; GENE; GRANULOCYTE; MACROPHAGE; MONOCYTE; NATURAL KILLER (NK) CELL; PHAGOCYTE; PHAGOCYTOSIS; T-CELL LYMPHOCYTE.

mucosa-associated lymphoid tissue (MALT) A loosely organized collection of LYMPH tissue that underlies and integrates with epithelial tissue (the lining of mucous membranes) throughout the body. MALT reinforces the body's immune presence and response in areas of the body that provide direct interface with the external environment. These areas, such as the gastrointestinal tract and the LUNGS, are most vulnerable to breaches that could allow pathogens to enter the body to cause INFECTION.

MALT contains clusters of phagocytic cells such as macrophages and dendritic cells, which consume cellular debris, as well as T-cell lymphocytes and B-cell lymphocytes. T-cell lymphocytes attack and kill invading pathogens, and B-cell lymphocytes produce antibodies to protect against future invasion by the same pathogens. There are several types of MALT; each has specific functions, according to its location in the body. Among them are

- BRONCHUS-ASSOCIATED LYMPHOID TISSUE (BALT), which strengthens the body's defense against INFLUENZA and PNEUMONIA
- GUT-ASSOCIATED LYMPHOID TISSUE (GALT), which helps protect against invasion by gastrointestinal viruses
- NOSE-ASSOCIATED LYMPHOID TISSUE (NALT), which intensifies the body's resistance to airborne viruses such as those that cause COLDS
- SKIN-ASSOCIATED LYMPHOID TISSUE (SALT), which helps block BACTERIA, fungi, and other pathogens from passing through microscopic breaks in the SKIN
- VASCULAR-ASSOCIATED LYMPHOID TISSUE (VALT), which infiltrates the epithelium of the BLOOD vessels

MALT may be the site of solid tumors that develop in LYMPHOMA (sometimes called MALT lymphoma). The most common MALT site for such an occurrence is the gastrointestinal tract. Researchers believe these lymphomas develop when a constant assault, such as a persistent infection, engages the MALT site. B-cell lymphocytes accumulate to fight the infection. When their accumulation persists over time, which is abnormal, the B-cell lymphocytes turn cancerous. The connection with MALT lymphomas that arise from GALT is *HELICOBACTER PYLORI* infection, which also has a strong connection to STOMACH CANCER. Researchers believe *H. pylori* may account for 85 percent or more of gastrointestinal MALT lymphomas, many of which grow in the STOMACH. Treatment is highly successful when the diagnosis of MALT lymphoma occurs early in the CANCER's development because the tumors grow slowly and lack aggression in spreading.

For further discussion of MALT within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; B-CELL LYMPHOCYTE; FUNGUS; LYMPHOCYTE; MACROPHAGE; METASTASIS; MONONUCLEAR PHAGOCYTE SYSTEM; PATHOGEN; PHAGOCYTE; PHAGOCYTOSIS; T-CELL LYMPHOCYTE; VIRUS.

multiple chemical sensitivity syndrome A constellation of symptoms that result from exposure to common chemicals at levels that do not normally cause response or reaction. Multiple chemical sensitivity syndrome is difficult to diagnose and treat. Symptoms are often broad ranging. There remains disagreement among medical experts (doctors and researchers) about the diagnostic criteria and causes of the syndrome. Some believe multiple chemical sensitivity syndrome is a component of GENERALIZED ANXIETY DISORDER (GAD)

or PANIC DISORDER. Others believe it is a HYPERSENSITIVITY REACTION. Symptoms of multiple chemical sensitivity syndrome often include

- PALPITATIONS and CHEST PAIN
- fatigue and shortness of breath (DYSPNEA)
- difficulty sleeping
- cognitive disturbances

The diagnostic path is primarily clinical, based on the person's symptoms. Though BLOOD tests can detect changes in immune indicators such as IMMUNOGLOBULIN levels, LEUKOCYTE activity, and complement factors, the changes are inconsistent from one person to the next and do not necessarily correlate either to symptoms or exposures.

Treatment is avoidance, whenever possible, of environments and circumstances that exacerbate symptoms. Because the substances and their quantities or exposures to them are common, however, it is often hard for the person to avoid exposure. Medications typically given to treat hypersensitivity reactions, such as ANTIHISTAMINE MEDICATIONS or CORTICOSTEROID MEDICATIONS, do not relieve the symptoms and discomforts of multiple chemical sensitivity syndrome. For most people the syndrome is chronic, with symptoms waxing and waning. Multiple chemical sensitivity syndrome can have a significant affect on QUALITY OF LIFE.

See also CHRONIC FATIGUE SYNDROME; COGNITIVE FUNCTION AND DYSFUNCTION; COMPLEMENT CASCADE; FIBROMYALGIA.

N

natural killer (NK) cell A granular LYMPHOCYTE (white BLOOD cell with granules in its cytoplasm) that has cytotoxic (cell-killing) functions within the IMMUNE RESPONSE. NK cells belong to the CELL-MEDIATED IMMUNITY pathway of the immune response and do not require ANTIGEN presentation to target a cell for destruction. NK cells are particularly involved in killing tumor cells. They release molecules that puncture or perforate (make molecular holes in) the cell membrane of the cell under attack. This assault may directly kill the cell or cause accelerated APOPTOSIS (planned cell death) that the target cell itself initiates in response to the damage it experiences.

For further discussion of natural killer cells within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY-MEDIATED IMMUNITY; B-CELL LYMPHOCYTE; MACROPHAGE; T-CELL LYMPHOCYTE.

nonsteroidal anti-inflammatory drugs (NSAIDs) Medications that relieve INFLAMMATION by suppressing the action of PROSTAGLANDINS, which are responsible for the inflammatory response. There are several types of prostaglandins, most of which are biochemical messengers that have numerous roles in routine cellular activity. Other prostaglandins are the agents of inflammation. The prostaglandins that incite inflammation do so by summoning numerous other biochemicals to the site of an injury, ultimately resulting in fluid accumulation and swelling at the site.

Three NSAIDs are available in over-the-counter (OTC) preparations as well as stronger prescription-only products: ibuprofen, naproxen, and ketoprofen. All other NSAIDs available in the United States (except aspirin) require a doctor's prescription.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)	
aspirin	diclofenac
diflunisal	etodolac
fenoprofen	flurbiprofen
ibuprofen	indomethacin
ketoprofen	meclofenamate
mefenamic acid	meloxicam
naproxen	oxaprozin
nabumetone	piroxicam
sulindac	tolmetin

How These Medications Work

NSAIDs work by blocking the action of cyclooxygenase (COX), the enzyme that allows cells to convert arachidonic acid (a dietary fatty acid found in meats) into prostaglandins. The two main forms of COX are cyclooxygenase 1 (COX-1) and COX-2. Many types of cells in the body contain COX-1, but COX-2 occurs primarily in mast cells. COX-1 is responsible for prostaglandin synthesis for these roles. Prostaglandins are also the agents of inflammation. Mast cells contain COX-2, which enables them to synthesize large quantities of prostaglandins during an IMMUNE RESPONSE.

Most NSAIDs are nonselective; they block both COX-1 and COX-2. Though this action effectively relieves inflammation and associated symptoms (such as PAIN and FEVER), it also interferes with various general functions of cells throughout the body. One consequence of this interference is STOMACH upset. Gastric cells contain an abundance of COX-1 and synthesize forms of prostaglandin that help protect the lining of the stomach. Suppressing COX-1 activity reduces this protection. As

well, the NSAID preparations are generally acids, which further irritate stomach tissues.

Therapeutic Applications

Doctors prescribe or recommend NSAIDs for pain relief and to reduce fever and inflammation, such as from musculoskeletal injuries. NSAIDs have widespread therapeutic applications and are among the most commonly used medications in the United States. Though all NSAIDs share the same mechanism of action, some are more effective for specific conditions. Ibuprofen, naproxen, and ketoprofen are effective for general relief. Other NSAIDs more aggressively block COX, making them especially useful for moderate OSTEOARTHRITIS, RHEUMATOID ARTHRITIS, and inflammatory disorders such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).

The original NSAID is aspirin, first isolated and used as a therapeutic preparation in the late 1800s. Aspirin, a nonselective COX inhibitor, remains the most commonly used medication in the world, primarily for its ability to relieve pain and fever. In the 1970s cardiologists began recommending daily aspirin for people at high risk for HEART ATTACK. During an inflammatory response prostaglandins combine with other substances to make the surfaces of platelets (clotting cells) sticky. This encourages PLATELET AGGREGATION, the first step of COAGULATION (clot formation). Blocking prostaglandin synthesis reduces the likelihood for BLOOD clots to form in the blood vessels. This effect is unique to aspirin among the NSAIDs; other NSAIDs have only very mild antiplatelet effect.

In the late 1990s and early 2000s several selective COX-2 NSAIDs became available. These COX-2 inhibitors had the ability to selectively target and block only COX-2, allowing COX-1-mediated prostaglandin synthesis to continue unimpeded while preventing COX-2-mediated synthesis to reduce inflammation. However, widespread use of COX-2 inhibitors revealed that these medications carried increased risk for heart attack, and several were withdrawn from the US market. Nonselective (classic) NSAIDs do not appear to carry the same risk, though may increase the risk for heart attack in people who have recently had OPEN HEART SURGERY.

People who have recently had OPEN HEART SURGERY or HEART ATTACK should check with their doctors before taking any nonsteroidal anti-inflammatory drug (NSAID) preparation, including cold and flu products that contain an NSAID.

Risks and Side Effects

The most common risk of NSAIDs is gastric upset and PEPTIC ULCER DISEASE. Extended use of an NSAID diminishes the amount of prostaglandins in the stomach, reducing the ability of the gastric mucosa (stomach lining) to protect itself from the acid normally present in the stomach as well as the acid of the NSAID itself. Some NSAIDs have more of this affect. Other common side effects include allergic reaction and interaction with other drugs. NSAIDs interact with numerous drugs as well as with each other. TINNITUS (ringing in the ears) is an early indication of excessive NSAID consumption. Long-term, high-DOSE NSAID use can cause permanent kidney and LIVER damage and failure of these organs.

See also ASPIRIN THERAPY; CORTICOSTEROID MEDICATIONS; DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS); DRUG INTERACTION; EAR; IMMUNOSUPPRESSIVE MEDICATIONS; KIDNEYS; LIVER FAILURE; MAST CELL; PLATELET; RENAL FAILURE.

nose-associated lymphoid tissue (NALT)

Loosely organized collections of LYMPH tissue embedded in the mucous membrane lining (mucosa) of the nasal passages and sinus cavities. Nasal mucous, which the nasal mucosa secretes, is one of the body's front-line protective mechanisms, providing a physical barrier that repels or traps foreign substances such as BACTERIA, viruses, toxins, and inhaled particles. Many pathogens gain entry to the body through the NOSE. NALT contains numerous B-cell lymphocytes and T-cell lymphocytes that detect and respond to invading pathogens. Macrophages, eosinophils, and other phagocytic cells are also concentrated in NALT to clean up cellular debris that NALT traps or collects.

The mucous membrane lining of the nose is the first point of contact for inhaled allergens. Its mast

cells quickly initiate an IMMUNE RESPONSE by releasing HISTAMINE and other biochemicals to stimulate LYMPHOCYTE activity. This HYPERSENSITIVITY REACTION results in the common symptoms of ALLERGIC RHINITIS (seasonal allergies). In 2003 the US Food and Drug Administration (FDA) approved the first nasal VACCINE for INFLUENZA (the flu). It was the first to capitalize on the immune response NALT can generate to provide systemic (bodywide) IMMUNITY for the influenza strains the vaccine contains.

For further discussion of NALT within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ALLERGEN; B-CELL LYMPHOCYTE; BRONCHUS-ASSOCIATED LYMPHOID TISSUE (BALT); COLDS; MACROPHAGE; MAST CELL; MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); PATHOGEN; PHAGOCYTE; SKIN-ASSOCIATED LYMPHOID TISSUE (SALT); SNEEZE; VASCULAR-ASSOCIATED LYMPHOID TISSUE (VALT); VIRUS.

P–R

partial combined immunodeficiency (PCID) An immune disorder in which the IMMUNE SYSTEM is missing key components. Most often people who have PCID lack certain leukocytes (white BLOOD cells), which impairs their ability to form antibodies (develop IMMUNITY) and fight INFECTION. The abnormality might be with cell differentiation, maturity, or function. Sometimes PCID involves deficits of complement factors, the specialized proteins that activate ANTIBODY–ANTIGEN binding. Symptoms of PCID vary somewhat, depending on the immune deficit though generally include frequent infections and autoimmune reactions. Common infections are PNEUMONIA and CANDIDIASIS (thrush). OPPORTUNISTIC INFECTION may also occur. Autoimmune reactions often involve the SKIN, appearing as atopic DERMATITIS and other rashes.

The diagnostic path typically includes blood tests that measure the types and quantities of white blood cells, IMMUNOGLOBULIN, and complement factors. GENETIC TESTING may identify the presence of GENETIC DISORDERS that have IMMUNODEFICIENCY components. Treatment varies according to the immunodeficiency and severity of symptoms, though usually includes ANTIBIOTIC MEDICATIONS to control infections and GAMMAGLOBULIN injections to bolster the IMMUNE RESPONSE.

See also ANTIBODY-MEDIATED IMMUNITY; CELL-MEDIATED IMMUNITY; COMMON VARIABLE IMMUNODEFICIENCY (CVID); COMPLEMENT CASCADE; IMMUNE DISORDERS; LEUKOCYTE; LIVING WITH IMMUNE DISORDERS; RASH; SEVERE COMBINED IMMUNODEFICIENCY (SCID).

passive immunity IMMUNITY (protection from INFECTION) that occurs without activation of the IMMUNE RESPONSE. A newborn has passive immunity from the antibodies in his or her mother's BLOOD at the time of birth and continues to receive limited ANTIBODY protection for the duration of BREASTFEEDING. Passive immunity also occurs when a person receives GAMMAGLOBULIN that contains antibodies present in the blood (PLASMA) of the donors who are the source for the gammaglobulin.

For further discussion of immunity within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ACTIVE IMMUNITY; INNATE IMMUNITY.

Peyer's patches Small, nodular clusters of lymphoid tissue scattered throughout the mucous membrane lining of the SMALL INTESTINE. Though not encapsulated as are LYMPH NODES, Peyer's patches are more distinct and organized than other MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT). Peyer's patches are elements of GUT-ASSOCIATED LYMPHOID TISSUE (GALT), a subset of MALT. GALT lies beneath the epithelial tissue (mucosal lining) of the gastrointestinal tract. Peyer's patches contain concentrations of B-cell lymphocytes that actively produce antibodies. They also contain some T-cell lymphocytes and phagocytic cells to enhance the IMMUNE RESPONSE in the small intestine.

For further discussion of Peyer's patches within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; B-CELL LYMPHOCYTE; LYMPHOCYTE; PHAGOCYTE; T-CELL LYMPHOCYTE.

prostaglandins A large family of fast-acting lipid mediators primarily responsible for initiating INFLAMMATION, FEVER, and PAIN during the IMMUNE RESPONSE. Prostaglandins are also vital for numerous functions throughout the body. Thromboxane, one of the prostaglandins, facilitates PLATELET

AGGREGATION to aid COAGULATION (BLOOD clotting). Other prostaglandins facilitate calcium transport to and from cells, the onset and progression of labor during CHILDBIRTH, and the functions of other hormones. Prostaglandins are also responsible for discomforts related to their release, such as after injury when inflammation results or when menstrual cramps (DYSMENORRHEA) occur.

Prostaglandin activity is autocrine (affects only cells that secrete it) or paracrine (affects cells within immediate proximity of the secreting cells). Prostaglandin activity is also intense but short lived, though the symptoms of the resulting inflammation continue for some time after prostaglandin release stops. Mast cells are the main source of prostaglandin synthesis and secretion. Epithelial cells (surface cells of the SKIN and mucous membranes) and platelets also produce as well as respond to prostaglandins.

PROSTAGLANDINS AND THE PROSTATE GLAND

The researchers who discovered prostaglandins in the 1930s isolated the first member of this biochemical family from SEMEN—the secretions of the PROSTATE GLAND. They named it for this connection. Over the following decades further research identified a number of prostaglandins and determined that nearly every cell in the body contains some form of prostaglandin. Aspirin was the first DRUG to block the synthesis of prostaglandins.

The enzymes cyclooxygenase 1 (COX-1) and COX-2 facilitate the synthesis of prostaglandins from arachidonic acid, an essential fatty acid (a fatty acid the body requires for health but cannot synthesize from other substances so must obtain from dietary sources) found in red meats and peanuts. Arachidonic acid is also the foundation for LEUKOTRIENES, other biochemicals also involved in the inflammatory response. The enzyme lipoxygenase facilitates the conversion of arachidonic acid to leukotrienes. COX-1 is primarily in the STOMACH, KIDNEYS, and walls of the blood vessels; it maintains the prostaglandins necessary for the body's normal functioning. COX-2 is present in the tissues and becomes active during an inflammatory response.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), including aspirin, block the action of COX, preventing prostaglandin production. This action provides pain relief, reduces fever, and mitigates the swelling associated with inflammation. Though much therapeutic focus is on blocking prostaglandin production, there are numerous therapeutic applications for synthetic prostaglandins. Therapeutic administration of synthetic prosta-glandin E_1 (PGE_1) maintains a patent ductus arteriosus in infants born with serious congenital heart defects. Prostaglandin E_2 (PGE_2) and prostaglandin F_2 (PGF_2) cause the UTERUS to contract, either initiating or strengthening labor.

See also CONGENITAL HEART DISEASE; CRAMP; HORMONE; IMMUNE RESPONSE; IMMUNOGLOBULIN; MAST CELL; PLATELET.

psychoneuroimmunology The interrelationships between emotions, neurologic function, and the IMMUNE SYSTEM. In the 1970s researchers discovered receptors for neuropeptides on cells throughout the body, including the immune system. The BRAIN produces neuropeptides, protein-based structures that convey biochemical messages related to cognition (thought and logic) and emotion. Neuropeptides include endorphins and enkephalins, substances connected to perceptions of SATIETY and pleasure.

Though researchers do not yet understand how neuropeptides affect IMMUNE RESPONSE, they do know emotional stress affects physical health. They also know that the immune system affects neurologic functions, which is one reason people feel irritable and cranky when they are sick. It appears that the primary messengers for immune-to-neural communication are the CYTOKINES immune cells produce during the immune response, notably INTERLEUKINS, which are capable of activating NERVE impulses that convey signals to the brain. Researchers continue to explore ways to use these connections for health, HEALING, and disease prevention.

See also MIND–BODY CONNECTION.

reticuloendothelial system See MONONUCLEAR PHAGOCYTE SYSTEM.

rheumatoid arthritis A chronic, autoimmune disorder in which nodules and INFLAMMATION develop within the synovial capsules of the joints, causing erosion of the BONE and connective tissues, eventually deforming the JOINT. Synovial membranes encapsulate the joints and secrete synovial fluid, which lubricates the structures of the joint so they move smoothly and freely against each other. The antibodies that characterize rheumatoid arthritis attack the cells of the synovial membrane, causing inflammation and an IMMUNE RESPONSE that treats the cells as though they were invaders. The repeated inflammation over time results in fibrosis (scarring) that destroys the ability of the cells to produce synovial fluid and constricts the movement of the joint.

About two million Americans have rheumatoid arthritis, two thirds of them women. Rheumatoid arthritis most commonly develops between the ages of 20 and 50, though can occur in children (juvenile rheumatoid arthritis). Although treatments and lifestyle strategies can reduce inflammation and relieve symptoms, at present there is no cure for rheumatoid arthritis.

IS IT RHEUMATOID ARTHRITIS OR OSTEOARTHRITIS?

Arthritis is any condition of INFLAMMATION that affects the joints. OSTEOARTHRITIS is the form most people identify; about 20 million Americans have osteoarthritis. Though both forms involve inflammation of the joints, the two conditions are quite different. In osteoarthritis inflammation occurs in response to damage, usually that of repeated wear and tear, within the joints. In rheumatoid arthritis, the inflammation occurs first as a malfunction of the IMMUNE RESPONSE and causes damage to the joints. Osteoarthritis is more common in people over age 65, whereas rheumatoid arthritis usually arises before age 50.

Symptoms and Diagnostic Path

The symptoms of rheumatoid arthritis typically include

- PAIN and swelling in the joints, especially the small joints of the hands and fingers
- stiffness in the joints, especially upon awakening or after long periods of inactivity
- low-grade FEVER
- fatigue and weakness
- rheumatoid nodules, painless bumps under the SKIN that develop at pressure points
- joint deformity as the disease progresses

The diagnostic path includes BLOOD tests to detect antibodies and other indications of inflammation. Many people who have rheumatoid arthritis have a specific ANTIBODY called rheumatoid factor, though not all people who have rheumatoid arthritis have this antibody, and conversely, rheumatoid factor may be present in people who do not have rheumatoid arthritis. Blood levels of C-REACTIVE PROTEIN also can indicate whether inflammation exists in the body. X-rays can help the doctor evaluate and monitor damage to the joints and bones.

Treatment Options and Outlook

Treatment typically blends lifestyle measures to protect affected joints from undue stress and medications to relieve inflammation and pain. Daily exercise and activity that puts each affected joint through its complete range of motion help keep SCAR tissue from contracting (tightening) within the synovial capsule, maintaining relative freedom of movement. Activities such as YOGA and TAI CHI also improve FLEXIBILITY, range of motion, and balance. Omega-3 fatty acids and folic acid may block steps in the inflammatory response that reduce its intensity. Stress management methods such as MEDITATION help people to cope with the challenges of a chronic health condition.

Mild rheumatoid arthritis symptoms, especially pain, often respond to NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). Acetaminophen may also relieve pain, though it does not reduce inflammation. Topical preparations such as capsaicin and complementary therapies such as ACUPUNCTURE and REIKI may provide relief from pain and other symptoms. Medications for moderate to severe symptoms may include CORTICOSTEROID MEDICATIONS, which suppress the inflammatory response, and DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS), which block the immune response in various ways, depending on the med-

ication. Combinations of medications often provide the greatest relief. Surgery to replace seriously damaged joints with prosthetic joints becomes a treatment option when other therapeutic approaches cannot contain symptoms.

MEDICATIONS TO TREAT RHEUMATOID ARTHRITIS

acetaminophen	adalimumab
anakinra	aspirin
azathioprine	cyclosporine
etanercept	gold salts
hydroxychloroquine	ibuprofen
infliximab	ketoprofen
leflunomide	methotrexate
methylprednisolone	naproxen
prednisolone	prednisone
sulfasalazine	

Risk Factors and Preventive Measures

Researchers believe rheumatoid arthritis develops when various genetic, environmental, and hormonal factors converge. But specific risk factors remain elusive. There are no known measures to prevent rheumatoid arthritis from developing. Early diagnosis and treatment of juvenile rheumatoid arthritis are important to maintain optimal joint structure, integrity, and function. Prevention efforts focus on minimizing the consequences that the inflammation of rheumatoid arthritis causes, to preserve joint function as well as QUALITY OF LIFE.

See also AUTOIMMUNE DISORDERS; CHONDROITIN; GLUCOSAMINE; JOINT REPLACEMENT; LIVING WITH IMMUNE DISORDERS; RHEUMATIC HEART DISEASE; SAME; SCAR; STRESS AND STRESS MANAGEMENT; VASCULITIS; X-RAY.

sarcoidosis An inflammatory disorder in which multiple granulomas (nodules of hardened LYMPH and fibrous tissues) form in organs and tissues throughout the body. Sarcoidosis most commonly affects the LUNGS, LIVER, lymph nodes, eyes, and SKIN, though can affect any body structure. The granulomas typically have alternating growth and REMISSION stages, though generally cause permanent scarring. Though most people who have sarcoidosis develop small granulomas and have mild symptoms, sarcoidosis can be severe when the granulomas clump together to form large enough lesions to interfere with an organ's functions. Sarcoidosis that affects the HEART can cause life-threatening ARRHYTHMIA with high risk for SUDDEN CARDIAC DEATH.

Symptoms and Diagnostic Path

Most often sarcoidosis begins in the lungs, causing pulmonary symptoms, and in the lymph nodes. Symptoms are specific for the organ system involved. Generalized symptoms may include

- fatigue, weakness, and malaise (general sense of not feeling well)
- weight loss and loss of APPETITE
- FEVER
- night sweats and sleep disturbances
- SPLENOMEGALY (enlarged SPLEEN)
- HEPATOMEGALY (enlarged liver)
- enlarged, tender lymph nodes
- HEADACHE
- ERYTHEMA NODOSUM (red, painful skin lesions most commonly appearing on the shins)

The diagnostic path begins with BLOOD tests, chest X-RAY, and pulmonary function tests (95 percent of people who have sarcoidosis have lung involvement). The doctor may conduct other diagnostic procedures, depending on the symptoms and the necessity to rule out other causes for them. Though various procedures can show characteristic evidence of sarcoidosis, there are no conclusive diagnostic tests for sarcoidosis. Imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN and MAGNETIC RESONANCE IMAGING (MRI) can reveal the extent of damage present as a consequence of the granulomas.

Treatment Options and Outlook

Long-term treatment (up to a year) with CORTICOSTEROID MEDICATIONS reduces the INFLAMMATION that causes symptoms and mitigates the consequential damage. Topical medications can improve skin symptoms. Severe or resistant symptoms may require IMMUNOSUPPRESSIVE THERAPY or IMMUNOTHERAPY. Even with treatment, sarcoidosis remains a chronic condition with alternating periods of remission (no symptoms) and exacerbation (resumed or intensified symptoms).

MEDICATIONS TO TREAT SARCOIDOSIS

azathioprine	cyclophosphamide
etanercept	hydroxychloroquine
infliximab	methotrexate
pentoxifylline	prednisone
tetracycline	thalidomide

Risk Factors and Preventive Measures

There are no clear risk factors for sarcoidosis, though it is more common and often more severe in African American women. Nor are there any known measures to prevent sarcoidosis from developing. Researchers believe many people have undetected sarcoidosis, making this inflammatory

disorder far more common than doctors have long believed. Early diagnosis and treatment can minimize the consequences of the inflammation and fibrosis and allow improved QUALITY OF LIFE.

See also AUTOIMMUNE DISORDERS; EYE; GRANULOMA; IMMUNE DISORDERS; LIVING WITH IMMUNE DISORDERS; LYMPH NODE; OFF-LABEL USE; SCAR.

seasonal allergies See ALLERGIC RHINITIS.

severe combined immunodeficiency (SCID) A rare, genetic immune disorder in which an infant is born with severely deficient immune capability due to the absence of leukocytes. Because the infant receives PASSIVE IMMUNITY from his or her mother at birth (and through BREASTFEEDING), the deficiency often is not apparent until age three to six months or when the infant begins to receive routine immunizations. Doctors may suspect SCID if there are other family members who have IMMUNODEFICIENCY disorders. Most often the infant's immune status becomes suspect when there are recurrent or severe infections that a healthy IMMUNE RESPONSE would accommodate. Some babies develop deep abscesses, such as in the LIVER. Others have chronic OTITIS media (middle EAR INFECTION) or SINUSITIS (sinus infection).

Early diagnosis and treatment are essential. When doctors suspect and test for SCID within the infant's first three months of life, a BONE MARROW TRANSPLANTATION can provide the ability to produce lymphocytes, essentially curing the immunodeficiency. Most often, however, parents and doctors do not suspect an immune problem until the child is six months to a year old. By that time other features of the IMMUNE SYSTEM have developed enough to reject a BONE MARROW transplant unless IMMUNOABLATION first destroys the child's own bone marrow.

Bone marrow transplantation after age six months requires extended IMMUNOSUPPRESSIVE THERAPY to allow the new BLOOD STEM CELLS to take root and become self cells within the body. The child may also need ANTIBIOTIC PROPHYLAXIS and GAMMAGLOBULIN injections to bolster the immune response until the transplant fully takes hold. Without treatment SCID is fatal by two years of age and often in the first year of life. With bone marrow transplantation the child has a good chance for normal development and a relatively healthy life.

See also ABSCESS; COMMON VARIABLE IMMUNE DEFICIENCY (CVID); GENETIC DISORDERS; INHERITANCE PATTERN; LEUKOCYTE; LIVING WITH IMMUNE DISORDERS; LYMPHOCYTE; PARTIAL COMBINED IMMUNODEFICIENCY (PCID).

Sjögren's syndrome An autoimmune disorder that affects the glands that provide moisture for the mucous membranes, notably the lacrimal (tear) glands and the SALIVARY GLANDS. Sjögren's syndrome exists in one of three forms:

- primary, in which the only structures it affects are the exocrine glands and the main symptom is dryness
- secondary, in which Sjögren's syndrome appears in conjunction with another autoimmune disorder, typically RHEUMATOID ARTHRITIS, scleroderma, or SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
- ocular, in which symptoms affect only the eyes (lacrimal glands)

Symptoms and Diagnostic Path

Symptoms depend to some extent on the affected glands, which nearly always include the salivary glands and the lacrimal glands. The lack of moisture to the eyes can cause corneal ABRASIONS and PHOTOSENSITIVITY. However, symptoms may involve glands in mucous tissues throughout the body. Dryness affecting other mucous membranes may result in

- frequent nosebleeds (INFLAMMATION of the nasal passages)
- PERICARDITIS (inflammation of the membrane sac surrounding the HEART)
- BRONCHITIS (inflammation of the airways in the LUNGS)
- VAGINITIS (inflammation of the VAGINA)

There are no specific tests to diagnose Sjögren's syndrome. A Schirmer's test determines the moisture content of the eyes; salivary gland biopsy can reveal fibrosis and granulation typical of the inflammatory process. Doctors generally consider

the diagnosis conclusive when a person has three consecutive months of symptoms that include

- extremely dry MOUTH and swollen salivary glands
- dry, irritated membranes around the eyes and crusty accumulations on the eyelids
- inflammation of the joints

Treatment Options and Outlook

Treatment focuses on restoring moisture to the affected tissues. These efforts may include artificial tears EYE drops, moisturizing mouth rinses, vaginal moisturizing creams, and saline nasal sprays for the NOSE. Dental hygiene is crucial because the lack of saliva fosters the growth of BACTERIA and consequential DENTAL CARIES (cavities). Drinking water helps maintain moisture throughout the body. At present Sjögren's syndrome remains a chronic disorder for which there is no cure.

Risk Factors and Preventive Measures

Sjögren's syndrome affects predominantly women, with onset between the ages of 40 and 55. However, there are no known measures for preventing its development. Preventive measures instead focus on minimizing damage to the involved organ systems.

See also AUTOIMMUNE DISORDERS; CORNEA; DRY EYE SYNDROME; EPISTAXIS; LIVING WITH IMMUNE DISORDERS.

skin-associated lymphoid tissue (SALT) A loose organization of LYMPH cells and tissues that incorporates with the epidermis, the SKIN's living layer. The skin, as the body's primary interface with the external environment, is the foremost barrier to INFECTION. SALT, also called the skin IMMUNE SYSTEM (SIS), is very active. It contains large populations of mast cells, lymphocytes, and macrophages called Langerhans's cells. Its role is to intercept pathogens and other substances that manage to penetrate the physical barrier of the skin. These encounters are the basis for many of the antibodies the IMMUNE RESPONSE forms, particularly those related to allergies (HYPERSENSITIVITY REACTION).

Hypersensitivity reactions often involve dermatologic symptoms such as RASH and URTICARIA (hives). Numerous dermatologic conditions are IMMUNE DISORDERS or AUTOIMMUNE DISORDERS. Infections such as HIV/AIDS and HUMAN PAPILLOMAVIRUS (HPV) that deplete the systemic immune system result in reduced numbers of immune cells in SALT, increasing the skin's vulnerability to infection.

For further discussion of SALT within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; ANTIGEN; B-CELL LYMPHOCYTE; BRONCHUS-ASSOCIATED LYMPHOID TISSUE (BALT); INFECTION; KAPOSI'S SARCOMA; LYMPHOCYTE; MACROPHAGE; MAST CELL; MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); NOSE-ASSOCIATED LYMPHOID TISSUE (NALT); OPPORTUNISTIC INFECTIONS; PATHOGEN; PHAGOCYTE; T-CELL LYMPHOCYTE; VASCULAR-ASSOCIATED LYMPHOID TISSUE (VALT); VIRUS.

systemic lupus erythematosus (SLE) A chronic autoimmune disorder in which the IMMUNE RESPONSE creates antibodies that attack the cells of various organs. SLE is a type III HYPERSENSITIVITY REACTION (immune complex reaction) that most commonly develops between the ages of 15 and 40. Nine times as many women than men have SLE, and SLE is three times more common in African American women than women of other ethnicities.

Symptoms and Diagnostic Path

The symptoms of SLE vary widely in nature and severity and are often transient (come and go). Symptoms also vary depending on the affected organ systems, making it difficult to view them collectively as indications of a single disorder. The main symptoms of SLE may include

- characteristic "butterfly" RASH across the NOSE and onto the cheeks
- fatigue, often extreme
- painful and inflamed joints
- FEVER
- enlarged lymph nodes
- loss of HAIR
- CHEST PAIN, particularly with deep BREATHING or exertion
- sensitivity to sunlight

The diagnostic path is one of exclusion. It can take months to years for doctors to rule out other causes of the symptoms and settle on the suspicion of SLE. BLOOD tests that detect antinuclear antibodies (ANAs) suggest SLE. Many people who have SLE also have other antibodies, including anti-Ro and anti-La. However, not all do, and some people have these antibodies and do not have SLE. Some people who have SLE have decreased complement factors, though other conditions can cause the same finding.

Treatment Options and Outlook

Treatment incorporates various medications, singly or in combination, that target symptoms. The most commonly used medications are NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), antimalarial medications, CORTICOSTEROID MEDICATIONS, and IMMUNOSUPPRESSIVE MEDICATIONS. SLE is a chronic condition that medications can regulate to permit a relatively normal lifestyle. Stress exacerbates symptoms and precipitates flareups. Most people learn to identify when a flareup of symptoms is pending and to take appropriate interventions (medications and relaxation techniques) to mitigate their effects.

MEDICATIONS TO TREAT SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

cyclophosphamide	dexamethasone
hydrocortisone	hydroxychloroquine
ibuprofen	methotrexate
mycophenolate mofetil	naproxen
prednisone	

Risk Factors and Preventive Measures

The main risk factors for SLE are being female and being African American. Researchers do not know why gender and ethnicity influence the development of SLE. Preventive measures focus on reducing the complications of symptoms through prompt medical intervention and lifestyle practices, such as nutritious EATING HABITS and daily physical activity, that support health.

See also ANTIBODY; AUTOIMMUNE DISORDERS; DISCOID LUPUS ERYTHEMATOSUS (DLE); LIVING WITH IMMUNE DISORDERS; LYMPH NODE; MIND–BODY CONNECTION.

T-cell lymphocyte The type of white BLOOD cell (LEUKOCYTE) responsible for CELL-MEDIATED IMMUNITY. T-cell lymphocytes come to maturity in the THYMUS during childhood, which is why they are called T-cells. During the maturation process, T-cell lymphocytes "learn" how to recognize self and nonself antigens so they can distinguish between cells that belong to the body and cells that are foreign. Such a safeguard is necessary to keep T-cell lymphocytes from attacking the body's own cells. The thymus destroys lymphocytes that do not learn this distinction. After the thymus releases mature T-cell lymphocytes into the blood circulation, they differentiate into several subtypes. These include

- cytotoxic T-cell lymphocytes, also called killer T-cells or CD8 cells, which respond to nonself antigens to kill the cells that bear them
- helper T-cells, also called CD4 cells, which release CYTOKINES that stimulate B-CELL LYMPHOCYTE and cytotoxic T-cell lymphocyte activity
- memory T-cells, which carry specific antibodies and circulate in the blood for rapid activation should the same ANTIGEN reappear
- suppressor T-cells, which call off the IMMUNE RESPONSE when the threat to the body ends

The SPLEEN, the lymph nodes, and the MUCOSA-ASSOCIATED LYMPHATIC TISSUE (MALT) throughout the body contain millions of T-cell lymphocytes. T-cell lymphocytes also circulate in the blood and the LYMPH. T-cell lymphocytes may also be the source of disease, such as in HIV/AIDS (the VIRUS attaches to CD4 helper T-cells) and cutaneous T-cell lymphoma (CTCL), a form of cancer.

For further discussion of T-cell lymphocytes within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also ANTIBODY; ANTIBODY-MEDIATED IMMUNITY; CLUSTERS OF DIFFERENTIATION; LYMPH NODE; MAJOR HISTOCOMPATIBILITY COMPLEX (MHC); NATURAL KILLER (NK) CELL.

transforming growth factors (TGFs) CYTOKINES in the BLOOD circulation that attach to the surfaces

of cell membranes. Transforming growth factor alpha (TGF-alpha) stimulates the cells to grow, divide, and differentiate (cell proliferation). Lymphocytes and macrophages produce TGF-alpha. TGF-beta stimulates interleukin 1 (IL-1) production and blocks the response of lymphocytes in the inflammatory process. Lymphocytes, macrophages, and platelets secrete TGFs.

See also INFLAMMATION; INTERFERONS; INTERLEUKINS; LYMPHOCYTE; MACROPHAGE; PLATELET; TUMOR NECROSIS FACTORS (TNFS).

tumor necrosis factors (TNFs) CYTOKINES that kill tumor cells and participate in the inflammatory response. Leukocytes (white BLOOD cells) produce TNFs under stimulation from INTERLEUKINS. Tumor necrosis factor alpha (TNF-alpha), also called cachexin or cachectin, is the most active in these processes. Recombinant TNF-alpha is a treatment option for certain types of cancer. The spice turmeric (active ingredient curcumin) and the catechins in GREEN TEA also boost TNF-alpha. Overactive TNF production contributes to inflammatory AUTOIMMUNE DISORDERS such as RHEUMATOID ARTHRITIS and INFLAMMATORY BOWEL DISEASE (IBD). Doctors sometimes use therapeutic MONOCLONAL ANTIBODIES (MABS), such as infliximab and etanercept, to block TNF-alpha.

See also INFLAMMATION; LEUKOCYTE; RECOMBINANT DNA.

V

vaccine A substance that initiates an IMMUNE RESPONSE to produce antibodies that prevent INFECTION by the particular PATHOGEN. Vaccines contain attenuated live (weakened) or killed pathogens such as viruses or BACTERIA. The antigens of these pathogens activate the body's immune response, stimulating B-cell lymphocytes to produce antibodies specific to them. Genetic engineering makes it possible to produce large quantities of many vaccines in relatively short order. There are four types of vaccines:

- Attenuated vaccines contain live but weakened viruses to produce the strongest immune response. Laboratory manipulation of the VIRUS can establish narrow parameters of survival for the virus the vaccine carrier, such as temperature or acidity. These manipulations reduce the risk that the vaccine could cause infection, though such a risk exists. Often an attenuated vaccine requires only a single DOSE to establish full and long-term IMMUNITY.
- Inactivated vaccines contain killed bacteria or viruses. These pathogens still carry the antigens that will stimulate the immune response to produce antibodies but are incapable of causing infection. Though safer than attenuated vaccines, inactivated vaccines often require multiple doses or provide limited immunity.
- Acellular vaccines, also called subunit vaccines, contain particles of the virus or bacteria. These particles carry enough ANTIGEN to stimulate an immune response but are not complete enough to cause infection.
- Toxoid vaccines generate antibodies for the toxins certain bacteria generate when they cause infection. Tetanus and DIPHTHERIA are illnesses due to such toxins and the vaccines for them provide antibodies for the toxins rather than the bacteria that cause the illness.

Vaccines prevent many infectious diseases that were once major killers. Vaccination has essentially eliminated SMALLPOX worldwide, for example, and is close to eliminating POLIOMYELITIS. Some vaccines, such as for tetanus and pertussis, require multiple doses or periodic booster doses to establish full immunity. Because vaccines are effective for only the specific pathogens they contain, rapidly mutating pathogens such as the INFLUENZA virus require a new vaccine for each strain.

VACCINES

ANTHRAX	CHICKENPOX/shingles (varicella zoster viruses)
CHOLERA	diptheria, tetanus, acellular PERTUSSIS (DtaP)
DIPHTHERIA	HEPATITIS A (HAV)
Haemophilus influenzae type b (Hib)	INFLUENZA
hepatitis B (HBV)	MEASLES
LYME DISEASE	measles, MUMPS, RUBELLA (MMR)
meningococcal vaccine	pertussis
monkeypox	pneumococcal vaccine
mumps	RABIES
plague	rubella
POLIOMYELITIS	tetanus
rotavirus	typhoid
rubeola	
TUBERCULOSIS	
yellow FEVER	

Vaccines may not be effective in establishing immunity in people who are IMMUNOCOMPROMISED. Some people have allergies to the ingredients of the vaccine. Vaccines that contain attenuated live viruses sometimes use the preservative thimerosal,

which contains mercury. Because this heavy metal can cause neurologic damage, the United States has initiated a cooperative effort among vaccine manufacturers to develop thimerosal-free vaccines. Most recommended vaccines are now available without thimerosal or with minimal amounts of thimerosal.

People who travel should receive vaccines appropriate for the regions they intend to visit. The US Centers for Disease Control and Prevention (CDC) maintains a schedule of recommended travelers' immunizations at its Web site (http://www.cdc.gov).

See also ANTIBODY; ANTITOXIN; ANTIVENIN; B-CELL LYMPHOCYTE; CHILDHOOD DISEASES; INFLUENZA PREVENTION; LYMPHOCYTE; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

vascular-associated lymphoid tissue (VALT) Loosely collected clusters of LYMPH tissue throughout the inner, mucosal layer of the walls of the BLOOD vessels. Researchers discovered VALT in the late 1990s and remain unsure of its role and functions. There do appear to be correlations between LYMPHOCYTE activity in VALT and cardiovascular conditions such as ATHEROSCLEROSIS, which many cardiologists now believe results from an inflammatory process rather than creates INFLAMMATION. Researchers do not know, however, whether VALT attempts to fight the inflammation or contributes to it. Researchers are also investigating the relationship between VALT and dissecting aortic ANEURYSM, a life-threatening condition in which the layers of the walls of the abdominal AORTA begin to separate. The separations weaken the wall of this major ARTERY, creating substantial risk for the arterial wall to rupture.

For further discussion of VALT within the context of the structures and functions of the immune system, please see the overview section "The Immune System and Allergies."

See also BRONCHIAL-ASSOCIATED LYMPHOID TISSUE (BALT); GUT-ASSOCIATED LYMPHOID TISSUE (GALT); MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); NOSE-ASSOCIATED LYMPHOID TISSUE (NALT); SKIN-ASSOCIATED LYMPHOID TISSUE (SALT); VASCULITIS.

vasculitis A group of AUTOIMMUNE DISORDERS in which the epithelium (lining) of the BLOOD vessels becomes inflamed. The INFLAMMATION causes localized PAIN and swelling. There are numerous forms of vasculitis. They share common characteristics

TYPES OF VASCULITIS

Type of Vasculitis	Unique Symptoms	Treatment and Outlook
allergic granulomatosis and angiitis (Churg-Strauss syndrome)	primarily occurs in adults who have atopic bronchial ASTHMA affects BLOOD vessels of the LUNGS and musculoskeletal system eosinophilia (excessive number of eosinophils) and eosinophilic PNEUMONIA	CORTICOSTEROID MEDICATIONS sometimes resolves spontaneously though often is chronic course of disease may be progressive untreated eosinophilic pneumonia is life threatening
Behçet's syndrome	primarily occurs in adults who are in their 30s and is more common in men affects small arteries and veins serving epithelial tissue (SKIN and mucous membranes) and the eyes recurrent, painful ulcers in the MOUTH and VULVA that occur in clusters vision disturbances and UVEITIS inflammatory response with minor trauma such as scratches skin rashes	topical corticosteroid medications for mild skin symptoms colchicine, NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), dapsone, or thalidomide to control ulcerations IMMUNOSUPPRESSIVE MEDICATIONS for severe symptoms that do not respond to other treatments tends to be chronic with extended periods of REMISSION (several years) PHYSICAL THERAPY and physical exercise as tolerated to maintain joint FLEXIBILITY and range of motion

and symptoms though each of which has unique traits. Vasculitis may be acute (come on suddenly, run its course, and be over) or chronic (symptoms persist or come and go). Though vasculitis can affect any kind of blood vessel in the body, it most often involves arteries.

Symptoms and Diagnostic Path

Each type of vasculitis has unique symptoms. All types of vasculitis have in common these general symptoms:

- weight loss and loss of APPETITE

Type of Vasculitis	Unique Symptoms	Treatment and Outlook
giant cell arteritis (temporal arteritis)	primarily occurs in adults over age 50 affects arteries in the upper body, notably the neck and head (carotid network) severe HEADACHE, jaw PAIN, and scalp tenderness blind spots (scotoma), blurred vision, and other vision disturbances	high-DOSE corticosteroid medications for two to four weeks long-term corticosteroid therapy delayed treatment establishes high risk for blindness resulting from optic NEUROPATHY tends to be chronic
Henoch-Schönlein purpura	primarily occurs in children under age 6 purplish RASH on the legs and feet acute illness that lasts about 2 weeks affects blood vessels of the skin, joints, gastrointestinal tract, and KIDNEYS	complete recovery without treatment (self-limiting course of disease) possible complications, though uncommon, include RENAL FAILURE and GASTROINTESTINAL BLEEDING
hypersensitivity vasculitis (leukocytoclastic vasculitis)	affects small arteries in the skin, kidneys, gastrointestinal tract, lungs, and joints palpable (raised) PURPURA, commonly on the legs	corticosteroid medications or immunosuppressive medications when involvement is systemic symptoms can be recurrent
KAWASAKI'S DISEASE (mucocutaneous LYMPH NODE syndrome)	occurs primarily in children under age 5 acute onset with high FEVER lasting five days to two weeks fever does not drop with aspirin or acetaminophen inflamed and reddened eyes, reddened and chapped lips, peeling skin, and joint pain	high-dose, intravenous GAMMAGLOBULIN aspirin most children fully recover without complications risk for coronary ARTERY INFLAMMATION and aortic ANEURYSM requires lifelong monitoring for CARDIOVASCULAR DISEASE (CVD)
microscopic polyangiitis	more common in adults over age 50 affects arteries in the kidneys, skin, lungs, and that serve PERIPHERAL NERVES fever purpura and other skin rashes neuropathy and loss of NERVE function to feet and hands alveolar hemorrhage (bleeding into the tiny air sacs in the lungs)	corticosteroid medications in combination with immunosuppressive medications trimethoprim/sulfamethoxazole (antibiotic therapy)

Type of Vasculitis	Unique Symptoms	Treatment and Outlook
polyarteritis nodosa	affects arteries in the LIVER, gastrointestinal tract, kidneys purpura and skin ulceration pain in the joints and large muscles abdominal pain HYPERTENSION	aggressive, high-dose corticosteroid medications at diagnosis immunosuppressive medications for nonresponsive or severe symptoms long-term corticosteroid therapy to control chronic disease antihypertensive therapy untreated or severe disease has high risk for death complications include renal failure, LIVER FAILURE, and HEART FAILURE
polymyalgia rheumatica	primarily occurs in adults over age 60 severe pain and inflammation in the large joints (knees, hips, shoulders)	NSAIDs corticosteroid medications chronic symptoms requiring long-term treatment may indicate underlying giant cell arteritis
Takayasu arteritis	affects the AORTA and other large arteries most common in women between ages 20 and 35 pain and weakness in the back and arm on the affected side lower BLOOD PRESSURE in the arm on the affected side headache, dizziness, and vision disturbances hypertension	corticosteroid medications immunosuppressive medications for severe symptoms ANTICOAGULATION THERAPY such as aspirin or warfarin spontaneous resolution in about 95 percent of people possible complications include STROKE, HEART ATTACK, severe hypertension, aortic aneurysm, and heart failure
thromboangiitis obliterans (Buerger's disease)	most common in men aged 20 to 40 who smoke affects blood vessels in arms, hands, legs, and feet leg cramps with walking (INTERMITTENT CLAUDICATION) altered sensation or loss of sensation in feet (paresthesia) ulcerations on fingers and toes with rapid progression to GANGRENE (tissue death)	SMOKING CESSATION rest until inflammation subsides regular walking to improve circulation and muscular support for blood vessels aggressive treatment for ulcers that develop AMPUTATION of gangrenous digits or extremities chronic condition that requires diligent lifestyle management to minimize symptoms
Wegener's granulomatosis	more common in men over age 40 affects blood vessels in the NOSE, SINUSES, THROAT, lungs, and kidneys, often causing ulcerations chronic PNEUMONITIS chronic GLOMERULONEPHRITIS forms multiple granulomas	immunosuppressive medications corticosteroid medications with mild symptoms and early diagnosis trimethoprim/sulfamethoxazole (antibiotic therapy) treatment eliminates symptoms in 50 percent of people severe or untreated symptoms can be fatal outlook best with early diagnosis and treatment

- fatigue
- FEVER
- MUSCLE aches and PAIN
- JOINT pain and swelling

The doctor may conduct BLOOD tests to measure ANTIBODY types and levels, blood cell counts, and sedimentation rate and C-REACTIVE PROTEIN level (the latter two are indicators of inflammation in the body). Diagnostic imaging procedures such as Doppler ULTRASOUND, MAGNETIC RESONANCE IMAGING (MRI) COMPUTED TOMOGRAPHY (CT) SCAN, and angiogram can demonstrate any damage to or obstruction (blockage) of the arteries and veins. Sometimes a biopsy of the involved blood vessel is necessary to confirm the diagnosis.

Treatment Options and Outlook

Some types of vasculitis are self-limiting and do not require treatment. For most, treatment may include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), CORTICOSTEROID MEDICATIONS, and IMMUNOSUPPRESSIVE MEDICATIONS that have cytotoxic (cell-killing) effects (such as azathioprine and cyclophosphamide). The person may take one kind of medication or a combination of medications, depending on the symptoms and their severity. Nutritional EATING HABITS and daily physical exercise such as walking also aid HEALING and improved function.

Risk Factors and Preventive Measures

Doctors do not know what causes most vasculitis, though people who have autoimmune disorders are more likely to develop some type of vasculitis. Because some forms of vasculitis have potentially severe or life-threatening complications, early diagnosis and treatment are essential for optimal recovery or disease management. Many of the medications doctors prescribe to treat vasculitis have significant side effects such as OSTEOPOROSIS so it is important to be vigilant about such conditions.

See also ARTERY; ATHEROSCLEROSIS; HYPERSENSITIVITY REACTION; LIVING WITH IMMUNE DISORDERS; OPPORTUNISTIC INFECTION; RHEUMATOID ARTHRITIS; SYSTEMIC LUPUS ERYTHEMATOSUS (SLE); VEIN.

INFECTIOUS DISEASES

Infectious diseases are illnesses that result from INFECTION *with microorganisms, also called microbes. Doctors who treat people who have infectious diseases are internists (who treat adults) or pediatricians (who treat children) who subspecialize in infectious diseases.*

This section, "Infectious Diseases," presents an overview discussion of illness due to infection and entries about systemic infectious diseases (illnesses that affect the body as a whole), their treatments, and preventive measures. Other sections in *The Facts On File Encyclopedia of Health and Medicine* discuss infections specific to individual body systems.

Health, Infection, and Disease

An infection occurs when microbes—bacteria, fungi, parasites, viruses—and other pathogens (infectious agents) such as prions invade the body. The infection causes illness (becomes a disease) when it alters in some deleterious fashion the functions of the body. Some infectious diseases are primarily a health concern only to the people who have them, such as NECROTIZING FASCIITIS, TOXIC SHOCK SYNDROME, and CANDIDIASIS. These illnesses are noncommunicable; they do not spread to other people.

sIn some situations infections affect people who have no contact with one another but somehow share a generalized source of contamination. These infections, such as occur with WATERBORNE ILLNESSES in which drinking water or recreational water contains pathogens that people consume, or in LEGIONNAIRES' DISEASE, in which building heating and air-conditioning systems disperse *Legionella pneumophilia* bacteria to all who breathe the building's air, are communicable. Though contact among infected individuals may spread the infection, the typical mode of transmission is contact with the common source.

Numerous infections spread from one person to another, directly such as through touching or sharing bodily fluids or indirectly through sneezing or coughing. These illnesses are not only communicable but also contagious: they spread easily, rapidly, and often extensively. MEASLES, for example, is one of the most highly contagious communicable diseases; 90 percent of people exposed to the virus become ill with the disease. COLDS, infectious mononucleosis (EPSTEIN-BARR VIRUS infection), and INFLUENZA are among the most common contagious diseases in the United States.

Epidemics occur when large numbers of people become ill with a communicable or contagious disease. Throughout history these waves of infection decimated families, cities, countries, and even entire civilizations. Smallpox, measles, bubonic plaque, gonorrhea, syphilis, and influenza are among the infections that raged through populations. An infectious disease is endemic when it is always present at relatively the same rate of infection within a certain geographic region, environment, or population of people. Malaria is endemic in Africa, for example, and consistently sickens thousands of people.

Until the 1950s geographic boundaries confined most infectious diseases, not because pathogens (disease-causing microbes) had much regard for natural or national borders but because few people traveled very far from home. The advent of commercial air flight changed all that. By the 1970s air travel could whisk a person literally halfway around the world in less time than it

took to drive from San Francisco to Seattle. Few infectious diseases today remain localized, though the risk of infection with them varies widely. HIV/AIDS, SEVERE ACUTE RESPIRATORY SYNDROME (SARS), and INFLUENZA stand as stark evidence that microbes, too, travel the world.

CONTAGIOUS INFECTIOUS DISEASES

ANTHRAX	CHICKENPOX
CHLAMYDIA	COLDS
DIPHTHERIA	ENCEPHALITIS
GENITAL HERPES	GONORRHEA
HEMORRHAGIC FEVERS	HEPATITIS
INFLUENZA	MEASLES
MENINGITIS	MONONUCLEOSIS, INFECTIOUS
MUMPS	SCARLET FEVER
RUBELLA	STREP THROAT
SEVERE ACUTE RESPIRATORY SYNDROME (SARS)	SYPHILIS
TRICHOMONIASIS	TUBERCULOSIS
TYPHOID FEVER	

Infectious Diseases in Medical History

Infectious diseases have mystified and plagued humanity for ages. Tuberculosis, smallpox, cholera, typhoid FEVER, and the plague itself ("Black Death") were for centuries the leading causes of disability, disfigurement, and death. Mummified remains from ancient Egypt show evidence of smallpox and tuberculosis. Disfigurement resulting from smallpox was so common through the 18th century that artists routinely painted portraits that discreetly masked or simply did not portray the extensive scars the disease left on the faces of those who survived the illness. Hippocrates wrote of "phthisis"—Greek for consumption, an apt name for tuberculosis, the disease that slowly wasted away the lives of those infected. Manuscript fragments recovered from 7th century China reference measles. Ancient Greek documents record outbreaks of "pestilence" that were likely epidemics of measles, smallpox, and perhaps plague.

For centuries doctors believed infectious diseases like tuberculosis represented some sort of inborn weakness in a family because family members often had the same illness, generation after generation. Of course, doctors today know the true reason such illnesses affected entire families: infectious diseases like tuberculosis spread from person to person, and living in close contact makes it easier if not inevitable for them to spread.

The birth of vaccination and the death of a scourge In the summer of 1796, eight-year-old James Phipps became the first success story in an effort that would reach fruition nearly 200 years later. Country doctor Edward Jenner (1749–1823) made two scratches on the boy's arm with a lancet dipped in the fluid from a smallpox sore. Nothing happened. Not then, not 14 days later when the characteristic sores of smallpox should have started erupting. The scratches healed and James remained healthy.

Six weeks earlier, Jenner had performed a similar procedure using the fluid from a cowpox sore, a much milder form of illness that doctors today know develops from infection with a virus closely related to the virus that causes smallpox. Edward Jenner did not know this but had observed that milkmaids and farm hands who recovered from cowpox did not get smallpox. Young James became ill with cowpox, as Jenner expected he would, and then soon recovered—also as Jenner expected he would. Ironically, as an adult James Phipp nearly lost his life to another infectious disease endemic throughout history, tuberculosis.

In 1966 the World Health Assembly formalized a global smallpox eradication program with vaccination, Jenner's discovery, as its foundation. The first year of the program, 15 million people throughout the world contracted smallpox; nearly a third of them died. Ten years later, on October 26, 1977, Somalian Ali Mao Moallin became the last person in the world to acquire naturally occurring smallpox (he survived). In 1980, the World Health Organization officially declared smallpox eradicated worldwide and advised countries to end vaccination programs.

Today vaccination is the cornerstone of infectious disease control and preventive medicine. Vaccines confer IMMUNIZATION for numerous infectious diseases. Many countries, including the United States, routinely administer set schedules of vaccines to children, giving them lifelong immunity that protects them from infection with diseases such as POLIOMYELITIS, MUMPS, MEASLES, CHICKENPOX, RUBELLA, PERTUSSIS (whooping COUGH), and *Haemophilus influenzae* type b (Hib).

Microbes and the mechanisms of infection As early as the 16th century some scientists postulated the existence of unseen organisms as accountable for disease. The development of the microscope gave proof to the existence of such organisms; proving their connection to disease was more difficult. The first to succeed did so in a major way. German physician Robert Koch (1843–1910) isolated and cultivated *Mycobacterium tuberculosis*, the MICROBE responsible for the Western world's most pervasive and devastating disease. By the 19th century, tuberculosis infected so many people that it was more common than not. What puzzled doctors was why some people became ill and others did not.

Koch solved this mystery in 1882 when he demonstrated the ability of *M. tuberculosis* to cause tuberculosis infection. The methods of vaccination successful in preventing smallpox, anthrax, and other infectious diseases did not work with tuberculosis, however. Not until biochemist Selman Waksman (1888–1973) discovered streptomycin, a powerful antibiotic, in 1943 were doctors finally able to gain the upper hand against tuberculosis. Waksman received the Nobel Prize in Physiology or Medicine in 1952 for his work.

Through their work to understand a disease prevalent among livestock in the 19th century, foot-and-mouth disease, German researchers Friedrich Loeffler (1852–1915) and Paul Frosch (1860–1928) expanded the spectrum of pathogens. The pair postulated the existence of a particle smaller than bacteria caused the infectious disease. However, they lacked the technology to visualize such a particle. The development of the electron microscope in 1939 gave scientists the ability to see these smallest of infective agents, viruses.

Breakthrough Research and Treatment Advances Molecular medicine advances in the late 20th century gave another enormous boost to the fight against infectious diseases. In 1995 the bacterium *Haemophilus influenzae,* an insidious microbe responsible for numerous pulmonary and gastrointestinal diseases, became the first pathogen for which researchers unraveled the genetic code. The advance led to improvements in vaccines and treatments for *H. influenzae* infections as well as other bacterial diseases.

Molecular medicine also has provided tremendous breakthroughs in understanding the modus operandi of viruses such as HIV (human immunodeficiency virus), a Machiavellian retrovirus that subverts the immune system itself to perpetuate its own survival. These breakthroughs have paved the way for new antiviral medications that target specific molecular mechanisms of HIV, slowing its progress, and show promise for the development of a vaccine that can prevent HIV infection and AIDS.

As researchers gain insight into the adaptive mechanisms of pathogens such as bacteria and viruses, they are able to develop new drugs—and drugs that work in new ways—to treat the infections these pathogens cause. This is particularly important in light of the alarming rise in DRUG-resistant infections in diseases such as tuberculosis, GONORRHEA, and staphylococcal pneumonia. New viruses also threaten public health, placing renewed emphasis on vaccines and infection control measures to stop their spread. Though the control and eradication of many infectious diseases represent many of medicine's greatest triumphs, many of medicine's greatest challenges remain these same factors.

A

abscess A localized INFECTION containing pus, a fluid-based collection of white BLOOD cells, BACTERIA, and the debris resulting from the IMMUNE SYSTEM's efforts to fight the infection. Though an abscess may cause severe PAIN and compromise the function of organs in which it occurs, an abscess represents the success of the immune system to contain and enclose the infection. An abscess can develop anywhere in the body. Symptoms vary with the abscess's location though typically include pain and swelling in the area of the infection. There often is FEVER as well. An abscess on the SKIN or near the surface of the skin may form a red nodule or an open sore. Treatment is ANTIBIOTIC MEDICATIONS when the infection is bacterial. A deep, internal abscess may require surgery to drain the pus so HEALING can take place.

See also BARTHOLIN'S CYST; FURUNCLE; HEPATIC ABSCESS; LUNG ABSCESS; PERITONSILLAR ABSCESS.

adenovirus A VIRUS family that causes INFECTION of mucous membrane tissues throughout the body. Adenoviruses are responsible for a wide range of illness including upper respiratory infection, viral CONJUNCTIVITIS, GASTROENTERITIS, and URINARY TRACT INFECTION (UTI). These infections primarily affect children age 10 and younger. Infection with one adenovirus confers immunity to that strain of virus; vulnerability to infection with other strains of adenovirus remains. Adenoviruses are highly contagious and are particularly adept at mutating and adapting. They primarily spread through

- person-to-person direct contact, such as touching
- indirect contact, such as by touching doorknobs or furniture a person infected with the virus has touched, leaving viral particles behind, or by handling tissues an infected person uses
- airborne particles, such as enter the air via sneezing and coughing
- fecal contamination, such as through changing diapers or lack of HAND WASHING after using the bathroom

The INCUBATION PERIOD (time from exposure to onset of symptoms) is usually less than 10 days and often only 2 or 3 days. Adenoviral infection seldom causes serious illness and is self-limiting (goes away on its own after running its course). Symptoms depend on the location of the infection. The doctor may take mucus samples to test for the presence of BACTERIA, as the symptoms of bacterial and viral infections are often similar. Bacterial infection requires antibiotic therapy; ANTIBIOTIC MEDICATIONS are not effective against viral infections. Treatment for adenoviral infection targets symptom relief. Because adenoviruses are so pervasive, preventing infection is nearly impossible. The most important step to minimize the risk for infection is frequent hand washing with soap and warm water. People who are IMMUNOCOMPROMISED should avoid indoor crowds to the extent possible to reduce their exposure to people infected with adenoviruses.

See also COLDS; DIARRHEA; FOODBORNE ILLNESSES; SNEEZE/COUGH ETIQUETTE.

amebiasis A parasitic INFECTION of the gastrointestinal tract. The PARASITE responsible is *Entamoeba histolytica*, a single-cell organism (an ameba) that enters the body by drinking water or eating food that contains *E. histolytica* in cyst form. The cyst is a protective encasing within which the ameba

may sustain itself in a dormant stage for weeks to months outside a host (organism that provides NUTRIENTS for a parasite). Once within the SMALL INTESTINE the cyst ruptures and the ameba emerges to enter its active stage. In this active stage the ameba, called a trophozoite, travels to the COLON (large intestine) where it feeds on intestinal BACTERIA. As the population of trophozoites increases, they burrow into the intestinal mucosa (mucous lining of the colon). Substances trophozoites secrete to digest the substances they consume cause ulcerations (sores) that produce symptoms.

Symptoms and Diagnostic Path

The symptoms of amebiasis, also called amebic dysentery, begin two weeks to four months after ingesting the contaminated food or water. They include

- abdominal cramping or ABDOMINAL PAIN
- frequent bowel movements or DIARRHEA (which may be bloody)
- FEVER

The diagnostic path includes microscopic examination of stool samples to detect the presence of either cysts or trophozoites. The doctor may also conduct sigmoidoscopy to examine the colon for the characteristic ulcerations and to rule out other causes of the symptoms.

Occasionally trophozoites penetrate far enough into the intestinal mucosa to enter the BLOOD circulation, which transports them to other organs and extends the infection. The LIVER is the most common site for distant infection, where it presents as a HEPATIC ABSCESS, though the LUNGS and the BRAIN may also become involved. In locations other than the colon the trophozoites can cause abscesses, resulting in serious or life-threatening illness. Symptoms of systemic infection depend on the affected area.

Treatment Options and Outlook

Treatment for enteric or systemic infection is a combination of ANTIBIOTIC MEDICATIONS. Appropriate treatment cures the infection; inadequately treated or untreated amebiasis becomes chronic with cycles of alternating RECURRENCE and REMISSION of symptoms. Until recently doctors believed it was possible to have an *E. histolytica* infection without symptoms. However, although it is possible to have an *E. histolytica* infection with very mild symptoms, infectious disease specialists have determined a closely related and nearly identical ameba, *E. dispar*, is the cause of infection when no symptoms are present. *E. dispar* is benign and does not require treatment.

ANTIBIOTIC MEDICATIONS TO TREAT AMEBIASIS

diloxanide furoate	iodoquinol
metronidazole	paromomycin
tinidazole	

Risk Factors and Preventive Measures

Amebiasis is most common in countries where community sanitation is poor. People who travel in such countries or are immigrants to the United States from such countries, are at highest risk for amebiasis. The infection spreads through direct contact with fecal contamination, such as by eating vegetables from contaminated soil or drinking contaminated water. People who have amebiasis can spread the infection to other people. Diligent HAND WASHING and safe food preparation are effective measures for preventing the spread of amebiasis. Travelers to countries where sanitation is substandard should follow precautions that include eating only foods that are thoroughly cooked and drinking only bottled or canned beverages (without ice) or water boiled for a minimum of one minute.

See also BOWEL MOVEMENT; DRINKING WATER STANDARDS; FOODBORNE ILLNESSES; FOOD SAFETY; GASTROENTERITIS; PERSONAL HYGIENE; PROTOZOA; WATERBORNE ILLNESSES.

antibiotic medications Drugs that kill BACTERIA and certain other microorganisms. Antibiotic medications are the mainstay of treatment for bacterial INFECTION. Broad-spectrum antibiotics are capable of killing numerous types of bacteria; narrow-spectrum antibiotics kill specific types or strains of bacteria. There are seven primary classifications of antibiotic medications—aminoglycosides, cephalosporins, macrolides, quinolones (fluorquinolones), penicillins, sulfonamides, and tetracyclines—that contain over 100 different drugs.

COMMON ANTIBIOTIC MEDICATIONS

Aminoglycosides		
gentamicin	neomycin	tobramycin
Cephalosporins		
cefaclor	cefadroxil	cefepime
cefdinir	cefoperazone	cefoxitin
cefprozil	cefprozil	ceftazidime
cefuroxime	cephalexin	cephradine
loracarbef		
Macrolides		
azithromycin	clarithromycin	erythromycin
Quinolones (Fluoroquinolones)		
cinoxacin	ciprofloxacin	enoxacin
gatifloxacin	levofloxacin	lomefloxacin
moxifloxacin	nalidixic acid	norfloxacin
ofloxacin	sparfloxacin	trovafloxacin
Penicillins		
amoxicillin	amoxicillin/ clavulanate	penicillin V potassium
Sulfonamides		
cotrimoxazole	trimethoprim	trimethoprim/ sulfamethoxazole
Tetracyclines		
doxycycline	minocycline	tetracycline

How These Medications Work

Antibiotics are either bacteriocidal (kill bacteria directly) or bacteriostatic (kill bacteria by preventing them from reproducing). Some antibiotics are effective against anaerobic bacteria (bacteria that thrive in low-oxygen environments) and others against aerobic bacteria (bacteria that require normal atmospheric oxygen concentrations to survive). Just as the strains of bacteria share common traits yet have distinguishing features, the antibiotics within a particular class have similarities and differences. Doctors match bacteria and antibiotic for greatest EFFICACY. Individual variations among people also influence antibiotic effectiveness.

Therapeutic Applications

Antibiotic medications are effective for treating bacterial infections. They have no effect on viral infections or fungal infections. Laboratory analysis of fluid or tissue samples, called culture and sensitivity, is usually necessary to determine whether an infection is bacterial. The analysis involves attempting to grow the bacteria in the laboratory, then determining which antibiotics can kill the bacteria. Types of bacteria are sensitive to specific classes of antibiotics, so knowing the general classification of the bacteria is generally sufficient for the doctor to prescribe an antibiotic medication that will kill it.

Risks and Side Effects

Antibiotic medications have numerous side effects, ranging from HYPERSENSITIVITY REACTION (allergy) to LIVER or kidney damage. Allergy to penicillin is the most common DRUG allergy. Some antibiotics diminish the effectiveness of oral contraceptives (birth control pills). Most antibiotics increase the possibility for fungal (yeast) infection because they disturb the balance of NORMAL FLORA. Common consequences of this effect are antibiotic-related DIARRHEA and oral or vaginal CANDIDIASIS (yeast infection of the mouth or vagina).

ANTIBIOTIC RESISTANCE is a significant concern. Numerous strains of bacteria have adapted to become resistant to the antibiotics commonly used to treat the infections they cause. Factors that contribute to antibiotic resistance include overprescribing of antibiotics and failure to take antibiotic medications for the full course of prescribed treatment. These factors expose bacteria to antibiotics without killing them, giving the bacteria opportunity to adapt in ways that block the actions of the antibiotics in future generations of the bacterial strain. It is essential to take antibiotic medications only when necessary and for the full course of treatment.

See also ANTIBIOTIC PROPHYLAXIS; ANTIFUNGAL MEDICATIONS; ANTIVIRAL MEDICATIONS.

antifungal medications Drugs that kill fungi (yeast). Antifungal medications are available for topical or systemic treatment. Some fungal infections require both. Antifungal medications work through various mechanisms to interfere with the ability of fungi to survive or reproduce. Broad-spectrum antifungal medications are effective for treating a variety of fungal infections; narrow-

spectrum antifungals are effective in treating specific fungal infections.

Topical preparations may be lotions, creams, ointments, sprays, powders, or suppositories. Oral preparations may be tablets and liquids to swallow. Oral preparations to treat fungal infections involving the MOUTH (THRUSH) may be liquids to swish around the mouth or tablets (troche or lozenge) to allow to dissolve in the mouth. A variety of topical antifungal medications is available as over-the-counter products that do not require a doctor's prescription. These products are to treat common fungal and yeast infections such as vaginal CANDIDIASIS and athlete's foot and jock itch (TINEA INFECTIONS).

COMMON ANTIFUNGAL MEDICATIONS

ciclopirox	clioquinol
clotrimazole	fluconazole
flucytosine	griseofulvin
itraconazole	ketoconazole
miconazole	naftifine
nystatin	oxiconazole
terbinafine	tolnaftate

Topical antifungal preparations may cause irritation to the SKIN or mucous membranes, though this is uncommon. Systemic antifungal medications may interact with other medications and have possible side effects that vary with the DRUG. It is important to tell the doctor or pharmacist of all health conditions and medications taken to treat them, including OVER-THE-COUNTER (OTC) DRUGS and herbal products, to minimize the risk for ADVERSE REACTION and DRUG INTERACTION.

See also ANTIBIOTIC MEDICATIONS; ANTIVIRAL MEDICATIONS; FUNGUS; INFECTION.

antiviral medications Medications to shorten the course and lessen the severity of illness due to viral INFECTION as well as reduce viral shedding to minimize contagiousness. Some antiviral medications are able to prevent viral infection from developing after exposure to the VIRUS. Antiviral medications mark a fine line because they must destroy viruses without damaging the cells that host them. Most antiviral medications accomplish such a task by substituting inactive molecules for key enzyme molecules in the virus's efforts to replicate.

Antiviral medications are the mainstay of therapy for HIV/AIDS. Doctors also use antiviral medications to treat viral infections such as CHICKENPOX, HERPES SIMPLEX, HERPES ZOSTER (shingles), GENITAL HERPES, INFLUENZA, and chronic HEPATITIS B. Antiviral medications have numerous and sometimes serious side effects that vary with the medication. It is important for the doctor to know all medications a person takes, including OVER-THE-COUNTER (OTC) DRUGS and herbal remedies, to minimize the risk for ADVERSE REACTION and DRUG INTERACTION.

COMMON ANTIVIRAL MEDICATIONS

acyclovir	adefovir
alpha-interferon	amantadine
famciclovir	foscarnet
lamivudine	oseltamivir
penciclovir	ribavirin
rimantadine	valacyclovir
zanamivir	

See also PREVENTIVE HEALTH CARE AND IMMUNIZATION; VACCINE.

anthrax An illness resulting from INFECTION with the bacterium *Bacillus anthracis*. Anthrax is a naturally occurring infection among wild and domestic livestock (such as cows, sheep, goats, and antelope). Anthrax is rare in people in the United States, though more common in people who live, work, or travel to countries where anthrax is more common in livestock. The BACTERIA can cause infection in people who are exposed to sick animals, such as workers on farms and in slaughterhouses. Ranchers and farmers in the United States vaccinate their livestock against anthrax. An anthrax VACCINE is also available for people.

Symptoms and Diagnostic Path

Symptoms of anthrax depend on the form of illness. Anthrax in people can take three forms:

- Cutaneous anthrax, which accounts for 95 percent of human anthrax infections, results when *B. anthracis* enters an opening in the SKIN, such as a small scratch, and causes ulcerated sores on the skin. It is highly treatable with ANTIBIOTIC MEDICATIONS and nearly everyone who receives

antibiotic therapy recovers without complications.

- Inhalation anthrax results when a person breathes *B. anthracis* into the LUNGS, where the infection causes life-threatening PNEUMONIA. Inhalation anthrax requires urgent intravenous antibiotic therapy and intensive medical care. It is difficult to avoid respiratory collapse and cardiovascular shock, which are often fatal.
- Gastrointestinal anthrax results from eating meat contaminated with *B. anthracis*. It causes NAUSEA, VOMITING (often bloody), FEVER, ABDOMINAL PAIN, and profuse DIARRHEA. Many people recover, but the illness can be life threatening.

The diagnostic path includes a comprehensive history of potential exposure to livestock or livestock products and BLOOD tests to identify the presence of characteristic antibodies. The doctor may also culture body fluids to look for *B. anthracis*.

Treatment Options and Outlook

Antibiotic therapy is the mainstay of treatment for all forms of anthrax. The earlier treatment begins, the more effective it is. Untreated anthrax in any form can be serious or fatal. A person who has anthrax cannot spread the infection to others, though health-care providers follow diligent infection control protocols when treating people who have anthrax.

ANTIBIOTIC MEDICATIONS TO TREAT ANTHRAX	
ciprofloxacin	doxycycline
levofloxacin	penicillin

Risk Factors and Preventive Measures

Exposure to potentially contaminated livestock or livestock products (meat, hides, fur) is the primary risk for naturally acquired anthrax. A vaccine to prevent anthrax is available; however, current guidelines recommend its administration only to people at high risk for exposure to *B. anthracis* or after suspected exposure to *B. anthracis*. Multiple doses over 18 months, with annual boosters, are required to establish and maintain IMMUNITY.

In the late 1990s anthrax emerged as a worldwide bioterrorism threat, with concern for the possibility of widespread infection after intentional contamination of the US mail with *B. anthracis* caused two dozen Americans to become ill with anthrax, five of whom died from the inhalation form. At present public health experts recommend the vaccine in combination with antibiotic therapy to prevent illness in people exposed to *B. anthracis*.

See also ANTIBODY; FOODBORNE ILLNESSES; SMALLPOX.

B

babesiosis An illness that results from INFECTION with the parasitic protozoan *Babesia microti*. Most people who have babesiosis do not have symptoms; the infection causes illness primarily in people who are IMMUNOCOMPROMISED or who have had SPLENECTOMY (surgical removal of the SPLEEN). The bite of the *Ixodes* tick, found in the northeastern United States, is the mode of transmission. Babesiosis is rare in other parts of the United States.

B. microti infects the erythrocytes (red BLOOD cells), causing alterations in their cell membranes that affect their ability to carry oxygen. Hemolytic ANEMIA is a key consequence of babesiosis. Symptoms may include FEVER, COUGH, and shortness of breath (DYSPNEA). The doctor uses blood tests to diagnose babesiosis. The tests show the damage to the erythrocytes and the presence of antibodies. Treatment with ANTIBIOTIC MEDICATIONS cures the infection. Rarely, a person may develop the life-threatening complication ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS).

ANTIBIOTIC MEDICATIONS TO TREAT BABESIOSIS

atovaquone	azithromycin
clindamycin	quinine sulfate

See also ANTIBODY; ERYTHROCYTE; GIARDIASIS; LYME DISEASE; PROTOZOA.

bacteria Single-cell microorganisms (microbes). Bacteria are the most ancient and primitive life forms known, with fossils dating back more than 3 billion years. A bacterium's structure is very simple, consisting of a rigid cell wall that supports and contains the cytoplasm, fragments of RNA, and a single strand of DNA within a nonencapsulated (unbordered) nucleus. Though bacteria are capable of independent existence, most require a symbiotic relationship with a host organism. The bacteria provide needed functions for the host in exchange for NUTRIENTS and safe haven.

Many types of bacteria exist in and on the body in just such a symbiotic partnership; these are part of the body's NORMAL FLORA. Bacteria in the gastrointestinal tract digest food, for example. *Bifidobacterium bifidum, Lactobacillus acidophilus,* and *Saccaromyces boulardii* are some of the more abundant bacterial families that reside in the small intestine. However, when normal flora bacteria are able to establish themselves in tissues other than their natural habitat or their numbers become abundant, they cause INFECTION. *Escherichia coli*, for example, are abundant normal flora in the COLON, where they work to prepare the residue of digestion for elimination from the body. *E. coli* also synthesize VITAMIN K, which is essential for COAGULATION (BLOOD clotting). When *E. coli* escape from their habitat, however, they cause infections such as VAGINITIS or URINARY TRACT INFECTION (UTI).

THE "BAD" *E. COLI*: O157:H7

The bacterial family *Escherichia coli* is extensive and ubiquitous—its many strains live in the gastrointestinal systems of nearly all animals. *E. coli* O157:H7, NORMAL FLORA in cattle, is a family member of great notoriety for the potential of severe illness it presents in people. The toxin this strain releases can destroy red BLOOD cells in such volume that the KIDNEYS fail, a condition called HEMOLYTIC UREMIC SYNDROME. *E. coli* O157:H7 enters the human food chain as a foodborne illness.

Bacteria that cause infection are pathogens. Most pathogenic bacteria exist in the natural envi-

ronment, they are harmful to human health, and the IMMUNE SYSTEM establishes mechanisms to stop, contain, or attack them should they enter the body. Bacteria can cause infection and illness by destroying the cells they invade or by releasing toxins. ANTIBIOTIC MEDICATIONS treat bacterial infections.

Traditional classification systems view bacteria according to their physical (morphologic) characteristics because these are the traits perceptible with the use of a microscope, the first tool available for viewing microbes. These characteristics provide basic information about the particular bacterial family that is important to doctors when choosing antibiotic medications to treat bacterial infections. Methods made available through advances in molecular medicine during the latter years of the 20th century, such as ribosomal analysis and DNA sequencing, allow improved understanding of how bacteria function both to support health and to cause illness.

ILLNESSES CAUSED BY BACTERIAL INFECTION

ABSCESS	ANTHRAX
APPENDICITIS	bacterial MENINGITIS
BOTULISM	CAMPYLOBACTERIOSIS
CHLAMYDIA	CHOLERA
COLD SORE	CONJUNCTIVITIS
DIPHTHERIA	EPIGLOTTITIS
FOLLICULITIS	FURUNCLE
GONORRHEA	HERPES ZOSTER
INFECTIOUS ARTHRITIS	LEGIONNAIRES' DISEASE
LISTERIOSIS	LYME DISEASE
MASTOIDITIS	NECROTIZING FASCIITIS
ORBITAL CELLULITIS	OSTEOMYELITIS
PERICARDITIS	PERITONSILLAR ABSCESS
PNEUMOCOCCAL PNEUMONIA	RHEUMATIC HEART DISEASE
ROCKY MOUNTAIN SPOTTED FEVER	SCARLET FEVER
SEPTICEMIA	STAPHYLOCOCCAL SCALDED SKIN SYNDROME
STREP THROAT	
SYPHILIS	TUBERCULOSIS
TYPHOID FEVER	

See also CELL STRUCTURE AND FUNCTION; CHILDHOOD DISEASES; *ESCHERICHIA COLI* INFECTION; NUTRITIONAL THERAPY; PATHOGEN.

botulism A potentially life-threatening illness resulting from INFECTION with the anaerobic bacterium *Clostridium botulinum*. The BACTERIA are naturally present in soil, where they encase themselves in spores. In the body, the bacteria release a toxin that blocks the release of acetylcholine, a NEUROTRANSMITTER that facilitates NERVE impulses from neurons to MUSCLE cells, causing PARALYSIS that may range in severity from mild to life-threatening. There are three types of botulism:

- Foodborne botulism results from eating improperly canned or cooked foods contaminated with *C. botulinum* spores. Because the bacteria are anaerobic, they thrive in the relatively oxygen-free environment of canned, bottled, or otherwise contained foods. Foodborne botulism most commonly causes gastrointestinal symptoms such as abdominal cramping and DIARRHEA, though can cause systemic symptoms that may include paralysis of the chest muscles.
- Wound botulism develops in traumatic injury wounds that close over after the injury, trapping bacteria within them. Usually the injury involves some sort of contact with soil. This type of botulism can result in the infection commonly called gas GANGRENE. Often treatment requires surgery to open and clean the wound, removing damaged and dead tissue, along with administration of intravenous ANTIBIOTIC MEDICATIONS.
- Infant botulism occurs in children under age one year whose gastrointestinal tracts are not fully developed. The most common source of *C. botulinum* that causes infant botulism is unpasteurized honey. In an older child or adult the NORMAL FLORA and environment of the gastrointestinal tract would neutralize the few *C. botulinum* spores honey typically contains, but the infant's system lacks the maturity to do this.

Symptoms and Diagnostic Path

Symptoms begin 2 to 10 days after exposure. Early neurologic symptoms include vision disturbances, difficulty swallowing and speaking, and drooping eyelids (PTOSIS). As the infection progresses, paralysis may develop throughout the body. In foodborne botulism symptoms also include NAUSEA, VOMITING, and diarrhea. In wound botulism, there may also be PAIN and swelling at the wound site though usually the wound appears normal.

The diagnostic path includes a comprehensive NEUROLOGIC EXAMINATION and testing for the presence of *C. botulinum* in either a stool sample or sample of the suspected food source.

Treatment Options and Outlook

Treatment in older children and adults is hospitalization and prompt administration of trivalent ABE ANTITOXIN to counter the effects of the toxin the *C. botulinum* bacteria produce. Additional treatment for wound botulism is intravenous antibiotics, usually high doses of penicillin or clindamycin. Treatment for infant botulism is the antibiotic amoxicillin. With prompt and appropriate treatment many people fully recover from botulism, though some people have weakness, paralysis, or other neurologic symptoms.

Risk Factors and Preventive Measures

C. botulinum spores are present in soil and thus can contaminate vegetables and fruits. The risk for infection occurs with improperly canned or processed foods because the *C. botulinum* bacteria thrive and vastly multiply in the anaerobic environment. It is not possible to detect their presence by the appearance, smell, or taste of the contaminated food, though often the can or jar lid bulges. Home-canned foods are more commonly the source of foodborne botulism. Infants under one year should not eat honey or foods that contain honey, as unpasteurized honey is a common source of *C. botulinum* spores that are not a health risk to adults but can cause illness in infants. Wound botulism may develop even when the person takes antibiotics because the broad-spectrum antibiotics typically prescribed are not effective against *C. botulinum*. Diligent cleansing of injuries that have soil contamination reduces the risk for wound botulism.

See also ANTIBIOTIC MEDICATIONS; BOTULINUM THERAPY; FOODBORNE ILLNESSES; FOOD SAFETY; GUILLAIN-BARRÉ SYNDROME; NEURON; WATERBORNE ILLNESSES.

C

campylobacteriosis An illness that results from INFECTION with the bacterium *Campylobacter jejuni.* The BACTERIA are commonly present in domestic birds such as chickens and turkeys without causing illness in the birds; the typical source of infection in people is undercooked poultry (especially chicken) or cross-contamination that occurs from improper handling and preparation of poultry. Health experts estimate that half the chickens slaughtered for market in the United States carry *C. jejuni*, though proper handling prevents cross-contamination and thorough cooking kills the bacteria so it does not cause infection. It is not possible to tell whether *C. jejuni* contaminates raw chicken; appropriate FOOD SAFETY measures are essential when preparing any poultry or meat. Other animal-based foods may also be the source of *C. jejuni*, nobly unpasteurized milk. Campylobacteriosis is one of the most common FOODBORNE ILLNESSES.

Symptoms and Diagnostic Path

Symptoms develop two to five days after consuming contaminated food or water and include DIARRHEA, abdominal cramping, and FEVER. Some people also have NAUSEA and VOMITING. The diarrhea may be slightly bloody. Many people do not seek medical treatment because the infection is self-limiting and generally runs its course in a few days. The doctor can positively identify *C. jejuni* as the culprit through cultures of stool samples, though this is not usually necessary.

Treatment Options and Outlook

Campylobacteriosis is self-limiting, with symptoms ending within five days. Most people who develop campylobacteriosis require only supportive treatment such as increased fluid consumption to prevent DEHYDRATION until the diarrhea runs its course. The doctor may prescribe an antibiotic medication such as erythromycin when symptoms are severe or recur. Rare complications of campylobacteriosis include GUILLAIN-BARRÉ SYNDROME, an autoimmune disorder that causes neurologic symptoms, including MUSCLE weakness and PARALYSIS. Though Guillain-Barré syndrome is rare, health experts believe campylobacteriosis triggers about 40 percent of cases.

Risk Factors and Preventive Measures

Proper food handling, thoroughly cooking chicken and other poultry, and drinking pasteurized milk are highly effective measures for preventing campylobacteriosis. Preventive food safety measures include

- wash hands with warm water and soap after handling raw poultry and meat
- use separate utensils, cutting knives, and cutting surfaces for preparing poultry and meats
- wash food preparation surfaces, knives, and utensils with hot water and soap immediately after using them

See also HAND WASHING; WATERBORNE ILLNESSES.

candidiasis An illness resulting from INFECTION with fungi (also called yeasts) from the *Candida* family, most commonly *Candida albicans,* though other *Candida* species may also cause infection. Candidiasis, commonly called yeast infection (or THRUSH when it involves the MOUTH), affects the mucous membranes of the mouth, ESOPHAGUS, urinary tract, or VAGINA. *Candida* may also affect the perineal area, such as in DIAPER RASH.

Yeasts and bacteria are NORMAL FLORA (microorganisms present in health) that keep each other in

balance. They are vital for numerous body functions such as digestion. Candidiasis develops when there is a disturbance of the balance that allows *Candida* to flourish, such as a change in the acid balance (pH) of the tissues, suppression of normal flora bacteria with antibiotic therapy, compromised immune function, and excessive moisture. Candidiasis is the most common cause of ESOPHAGITIS, VAGINITIS in women, and diaper rash in infants.

Chronic candidiasis may indicate an underlying health condition such as DIABETES and is often the first sign of HIV INFECTION. A doctor should conduct a comprehensive health examination in people who have four or more episodes of candidiasis in a year.

Symptoms and Diagnostic Path

Symptoms of candidiasis vary with the site of infection. In the mouth there are white patches on the tongue and inner cheeks (oral mucosa). Candidal vaginitis produces a characteristic "cheesy" discharge and intense itching. Candidal diaper rash appears as red, fragile blotches or sores with white pustules. In candidal esophagitis the doctor can see characteristic ulcerations on endoscopic examination. Invasive candidiasis may present with FEVER along with indications of LIVER disease such as JAUNDICE, neurologic impairment when infection involves the CENTRAL NERVOUS SYSTEM, cardiovascular compromise with candidal ENDOCARDITIS (infection of the lining of the HEART), or RENAL FAILURE when infection involves the KIDNEYS.

The diagnostic path for superficial (oral, esophageal, perineal, or genital) candidiasis includes taking samples of the white patches or discharge for examination under the microscope, which reveals the presence of abundant *Candida* colonies. BLOOD cultures show *Candida* growth in invasive candidiasis.

Treatment Options and Outlook

Superficial candidiasis is common and easily treatable with ANTIFUNGAL MEDICATIONS. HEALING occurs without residual consequences, though infection may recur when conditions are favorable. Invasive or systemic candidiasis, which occurs when the *Candida* enter the blood circulation, is a very serious infection that requires treatment with intravenous antifungal medications. Invasive candidiasis can be life-threatening in IMMUNOCOMPROMISED people.

ANTIFUNGAL MEDICATIONS TO TREAT CANDIDIASIS

amphotericin-B	clotrimazole
econazole	fluconazole
flucytosine	ketoconazole
micafungin	miconazole
nystatin	

Risk Factors and Preventive Measures

DIABETES, long-term use of CORTICOSTEROID MEDICATIONS, antibiotic therapy, and HIV/AIDS are among the key risk factors for candidiasis. A normal course of ANTIBIOTIC MEDICATIONS prescribed to treat bacterial infection may cause candidal vaginitis; women who are susceptible to vaginal candidiasis should discuss prophylactic antifungal therapy with their doctors. Preventive measures for candidal diaper rash, a consequence of both pH change (from URINE contact with the SKIN) and excessive moisture, include frequent diaper changes and application of protective cream or ointment to keep the perineal area clean and dry.

See also ENDOSCOPY; FUNGUS; OPPORTUNISTIC INFECTION; TINEA INFECTIONS.

carrier A person who has a bacterial or viral INFECTION but does not show symptoms or become ill because of the infection and yet can pass the infection on to other people. A third of people who have infectious HEPATITIS are carriers, for example. In some circumstances treating the infection eliminates it so the person cannot pass the infection to others. In other circumstances, such as hepatitis B VIRUS (HBV) infection, there is no effective treatment and the person is capable for life of transmitting the infection.

See also BACTERIA; GENETIC CARRIER; MODES OF TRANSMISSION; PARASITE.

chickenpox A common childhood illness that results from INFECTION with the varicella-zoster VIRUS, a member of the herpesvirus family. Chickenpox, also called varicella disease, is highly contagious, spreading through direct contact and

exposure to airborne droplets containing the varicella-zoster virus. The INCUBATION PERIOD (time from exposure to illness) is 10 to 21 days.

Symptoms and Diagnostic Path

The first symptoms are general and include FEVER, HEADACHE, loss of APPETITE, and sometimes NAUSEA and VOMITING. Within two days the characteristic pox emerge. These fluid-filled blisters cover the body and sometimes even occur within the MOUTH, on the surface and sometimes the inside of the eyelids, and in the VAGINA. The blisters itch intensely. In two or three days the fluid within the blisters oozes out and a crust forms, after which the itching subsides. However, new batches of blisters may continue to emerge in clusters for three to five days after the first outbreak.

Diagnosis is straightforward as the pox are characteristic and the illness is so highly contagious that it affects large numbers of people. Many health-care providers do not want to see people who are likely to have chickenpox because of the contagiousness and because treatment is supportive, not therapeutic. The person is contagious from two days before the onset of symptoms until all the pox crust over.

Treatment Options and Outlook

Most people do not require treatment other than supportive care to improve comfort. Such care may include

- calamine lotion applied to the blisters to relieve itching
- oral ANTIHISTAMINE MEDICATION to relieve itching
- acetaminophen or NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen to relieve headache, fever, and general discomfort
- tepid baths with oatmeal in the water to relieve itching

Isolation is important until all the pox have blistered. Schools may require children to remain home until the crusts are no longer apparent. Most people recover and are able to return to normal activities within 7 to10 days. The pox heal without scarring unless they become infected, which may happen with excessive scratching.

Do not give aspirin to anyone who has chickenpox, as doing so creates the risk for developing REYE'S SYNDROME. Reye's syndrome is a serious neurologic condition that can be fatal.

ANTIVIRAL MEDICATIONS can significantly lessen the severity and length of illness when taken within 24 hours of the first pox. However, doctors typically reserve antiviral medications for people at risk for severe illness—infants under one year of age, pregnant women, and people who are IMMUNOCOMPROMISED—because the normal course of illness is short and has very low risk for significant complications. The most common complication of chickenpox is bacterial infection of the pox that results from scratching, which introduces BACTERIA into the blisters. Complications that are rare though possible include ENCEPHALITIS, PNEUMONIA, and REYE'S SYNDROME.

The varicella-zoster virus remains in the body after the illness of chickenpox runs its course, retreating to the NERVE roots where it apparently enters a stage of dormancy. In 90 percent of people the virus never re-emerges; however, in about 10 percent of people the virus causes HERPES ZOSTER (shingles) years to decades after chickenpox.

Risk Factors and Preventive Measures

Exposure to the varicella-zoster virus is the only risk factor for chickenpox. It is very difficult to avoid exposure because the MODES OF TRANSMISSION are multiple. As well, the extremely contagious nature of the infection coupled with the extended incubation period means exposure often occurs before people realize they are ill; outbreaks of chickenpox are typically widespread. A VACCINE for chickenpox is part of the routine IMMUNIZATION schedule for children in the United States. The vaccine prevents chickenpox in about 85 percent of people who receive it and significantly reduces the severity and length of illness in those who acquire the infection.

See also BLISTER; CHILDHOOD DISEASES; MEASLES; MUMPS; OCULAR HERPES ZOSTER; PREVENTIVE HEALTH CARE AND IMMUNIZATION; RUBELLA; SNEEZE/COUGH ETIQUETTE.

chlamydia Illness resulting from INFECTION with the bacterium *Chlamydia trachomatis*. Chlamydia is one of the most common SEXUALLY TRANSMITTED DISEASES (STDS) in the United States, infecting an estimated three million people each year. However, fewer than a third seek treatment because their symptoms are mild or they do not have symptoms and do not know they have chlamydia. Half of men and two thirds of women who have chlamydia experience no symptoms, though they nonetheless pass the infection to their sex partners. Doctors sometimes call chlamydia the "silent STD" for this reason. A woman may also transmit chlamydia to her infant during vaginal childbirth.

Symptoms and Diagnostic Path

When symptoms are present, they generally appear within three weeks of exposure. Men may experience a discharge from the PENIS and PAIN with URINATION. Women may experience vaginal discharge and burning with urination in the early stages of infection, and later may have pelvic pain, low BACK PAIN, discomfort or pain with SEXUAL INTERCOURSE, and vaginal bleeding between periods.

The diagnostic path includes a physical examination (with PELVIC EXAMINATION for women) and laboratory testing of discharge samples to detect the presence of *C. trachomatis* bacteria. Because chlamydia often does not cause symptoms, diagnosis may occur as a consequence of ROUTINE MEDICAL EXAMINATION.

Treatment Options and Outlook

Treatment is with oral (by MOUTH) ANTIBIOTIC MEDICATIONS. It is important for sex partners to also receive treatment because when they do not, reinfection will occur. Appropriate antibiotic therapy eliminates the infection. People who receive treatment recover fully. However, scarring and other damage that occurs because of long-term infection in a woman is typically permanent, and can result in INFERTILITY.

Untreated chlamydia has significant consequences for women, about half of whom develop PELVIC INFLAMMATORY DISEASE (PID). PID is a leading cause of ECTOPIC PREGNANCY and of infertility. The infection damages and scars tissue in the FALLOPIAN TUBES, blocking the pathway by which OVA (eggs) travel from the OVARIES to the UTERUS. Scarring may also affect the uterus, preventing implantation in the earliest stages of PREGNANCY. Untreated chlamydia increases a woman's risk for HIV infection.

ANTIBIOTIC MEDICATIONS TO TREAT CHLAMYDIA

amoxicillin	azithromycin
doxycycline	erythromycin
levofloxacin	ofloxacin

Risk Factors and Preventive Measures

Nearly all chlamydia infections in adults occur as a result of vaginal, oral, or anal sex with someone who has the infection. Women in particular often are reinfected after they receive treatment but their sex partners do not. Infants may acquire chlamydia from their mothers during birth and may develop chlamydial CONJUNCTIVITIS (infection of the tissues around the eyes) or PNEUMONIA. Safer sex practices, such as monogamous relationships and condom use, are the most effective measures for preventing chlamydia. Health experts recommend annual chlamydia screening for sexually active women who are under age 25 or have multiple sex partners.

See also GENITAL HERPES; GONORRHEA; HUMAN PAPILLOMAVIRUS (HPV); REITER'S SYNDROME; SCAR; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SYPHILIS.

cholera An illness resulting from INFECTION with the bacterium *Vibrio cholerae*. The BACTERIA release a toxin in the SMALL INTESTINE that disrupts the electrolyte balance, drawing vast amounts of water into the small intestine and causing sudden, profuse DIARRHEA. The diarrhea in turn causes severe DEHYDRATION. The incubation period (time from exposure to illness) is a few hours to a few days.

Cholera nearly always occurs in conditions of poor sanitation and is endemic (constantly present) in many areas of the world where community sanitation is chronically substandard. Infection results from drinking water contaminated with *V. cholerae*, eating raw shellfish harvested from contaminated water, or eating uncooked foods rinsed with contaminated water.

BLOOD TYPE AND CHOLERA SUSCEPTIBILITY

For reasons researchers do not understand, people who have BLOOD TYPE O have twice the likelihood of contracting cholera than others, and people who have blood type AB seldom become infected.

Though the profuse, watery diarrhea of cholera has a characteristic appearance and smell, the doctor may perform a stool culture to confirm the diagnosis. Treatment is oral rehydration solution (ORS) to replace the massive loss of fluid that occurs with the diarrhea, which can exceed a quart an hour. Doctors may prescribe tetracycline to shorten the course of illness when symptoms are especially severe, though most people recover with appropriate rehydration.

Cholera is rare in the United States, though people who travel to parts of the world where cholera is endemic are at risk for infection. Preventive measures include frequent HAND WASHING; drinking only bottled beverages or water purified through boiling, chlorination, or iodinization; and avoiding raw foods.

See also DRINKING WATER STANDARDS; WATERBORNE ILLNESSES.

coccidioidomycosis An illness resulting from INFECTION with the spores of the fungus *Coccidioides immitis*, which occurs naturally in the soil in desert environments, inhaled into the LUNGS. Coccidioidomycosis affects the respiratory tract, primarily the lungs. About half of people infected with *C. immitis* do not become ill. The IMMUNE SYSTEM can successfully neutralize small numbers of *C. immitis* spores before they cause illness, though the person will test positive for infection. Exposure to high numbers of spores is more likely to result in illness. Among those who develop symptoms of coccidioidomycosis, commonly called valley FEVER, illness may be acute, chronic, or disseminated. In people who are IMMUNOCOMPROMISED, coccidioid omycosis may occur as an OPPORTUNISTIC INFECTION.

Symptoms and Diagnostic Path

The most common form of coccidioidomycosis is acute, in which symptoms develop within four weeks of exposure. Symptoms include

- nonproductive (dry) COUGH and CHEST PAIN
- FEVER
- fatigue
- chills and night sweats
- diminished APPETITE and weight loss
- HEADACHE
- MUSCLE and JOINT PAIN
- RASH
- LYMPHADENOPATHY (swollen LYMPH nodes)

The diagnostic path includes chest X-RAY and coccidioidin SKIN test. The skin test is positive 21 days after exposure. BLOOD tests may also show elevated antibodies.

Treatment Options and Outlook

Though the infection is self-limiting and resolves within three to six months without treatment in most people, doctors often prescribe ANTIFUNGAL MEDICATIONS to eradicate the infection more quickly and reduce the likelihood for complications, which may include MENINGITIS. Most people recover without residual effects. Some people develop chronic infection, in which symptoms recur. About 1 percent of people develop disseminated disease (also called progressive), in which the infection enters the blood circulation and travels to other structures and organs. Extended, sometimes lifelong, treatment with antifungal medications is required for chronic and disseminated coccidioidomycosis. People who are immunocompromised, take IMMUNOSUPPRESSIVE THERAPY, or are of Filipino or African American heritage have especially high risk for disseminated disease.

ANTIFUNGAL MEDICATIONS TO TREAT COCCIDIOIDOMYCOSIS

amphotericin B	fluconazole
itraconazole	ketoconazole

Risk Factors and Preventive Measures

The primary risk factor for coccidioidomycosis is exposure to soil, especially dust, containing *C. immitis* spores. Public health officials often note spikes in reported infections after desert dust storms. Farm and ranch workers, construction workers, and archaeologists have increased risk

for infection through continued exposure to soil and dust.

See also ASTHMA; BRONCHITIS; HISTOPLASMOSIS; PLEURAL EFFUSION; PNEUMONIA.

colds Common illnesses resulting from INFECTION with one of more than 200 variations of rhinovirus, a family of highly contagious viruses that infiltrate the nasal mucosa (mucous membranes that line the inside of the NOSE and the SINUSES). Because so many variations of rhinovirus can cause colds, most people get several colds a year. Children may get 8 to 10 colds in a year; adults may get half as many. Colds are the most common viral infections.

Symptoms and Diagnostic Path

The characteristic symptoms of a cold affect the nose and sinuses and represent the IMMUNE SYSTEM's efforts to rid the body of the VIRUS rather than the actions of the virus itself. Symptoms of a cold include

- runny nose (rhinitis) and sinus congestion
- sneezing
- yellowish green nasal discharge

Some people develop sore THROAT (PHARYNGITIS) and COUGH as a consequence of postnasal drip, and the sinus congestion often causes HEADACHE. Colds do not typically cause FEVER or MUSCLE aches; these and other more extensive symptoms suggest a different viral infection such as INFLUENZA (the flu). In children, EAR infections (OTITIS media) may occur as a secondary illness because the congestion clogs the eustachian tubes, causing fluid to accumulate in the middle ear.

Treatment Options and Outlook

Colds are self-limiting, generally running their course in five to seven days. Treatment is supportive, targeting relief of symptoms. Many over-the-counter (OTC) cold products contain decongestant medications, cough suppressants, ANALGESIC MEDICATIONS, and sometimes ANTIHISTAMINE MEDICATIONS. Drinking plenty of fluids is important to help loosen nasal secretions, particularly when taking decongestant medications that dry out the mucous membranes. Chicken soup, a time-honored folk remedy, may boost the immune system's efforts to fight the infective VIRUS. ANTIBIOTIC MEDICATIONS are *not* effective in treating viral infections. Doctors may prescribe ANTIVIRAL MEDICATIONS to people at risk for complications, generally those who are IMMUNOCOMPROMISED. Antiviral medications can shorten the course of the cold. Complications that may develop include BRONCHITIS and PNEUMONIA, both of which can have serious health consequences for people who lack a strong IMMUNE RESPONSE.

Risk Factors and Preventive Measures

Rhinoviruses are ever present. They tend to cause infection (colds) during times when people are together indoors for extended periods of time—winter. The rhinovirus particles travel through the air and attach themselves to surfaces such as doorknobs. The most effective measure for preventing colds is diligent HAND WASHING. Minimizing exposure to large crowds of people (such as in shopping malls, theaters, and restaurants) lowers the risk for exposure to viruses that cause colds. There is some evidence that the herbal product ECHINACEA can prevent or lessen the severity of colds. Zinc supplements boost immune function, helping the body resist infection with rhinoviruses.

See also ALLERGIC RHINITIS; EUSTACHIAN TUBE; SNEEZE/COUGH ETIQUETTE.

cryptococcosis An illness that results from INFECTION with the FUNGUS *Cryptococcus neoformans*, which is abundant in soil worldwide. Cryptococcosis may affect the MENINGES (membranes covering the BRAIN and SPINAL CORD), the LUNGS, or the SKIN. Infection is most likely in people who are IMMUNOCOMPROMISED and is a particular risk in those who have HIV/AIDS, Hodgkin's lymphoma, or SARCOIDOSIS. Though typically a mild and self-limiting illness, cryptococcosis disseminate (become widespread throughout the body).

Most people have mild, generalized symptoms of illness such as HEADACHE, muscle aches, COUGH, and chest tightness. Significant exposure to *C. neoformans* or compromised immune function causes more severe symptoms. Culture of body fluid samples provides definitive diagnosis. Mild cryptococcosis does not require treatment and most people recover without complications. Doctors prescribe

ANTIFUNGAL MEDICATIONS to treat severe symptoms or cryptococcosis in people who are immunocompromised (including those who have HIV/AIDS); long-term treatment may be necessary.

ANTIFUNGAL MEDICATIONS TO TREAT CRYPTOCOCCOSIS		
amphotericin B	fluconazole	flucytosine

See also CANDIDIASIS; COCCIDIOIDOMYCOSIS; CRYPTOSPORIDIOSIS; OPPORTUNISTIC INFECTION.

cryptosporidiosis An illness that results from INFECTION with the PARASITE *Cryptosporidium parvum,* which lives in the gastrointestinal tract of numerous animals and passes into the environment, primarily bodies of fresh water such as rivers and lakes, through the feces. The parasites form cysts that are highly resistant even to chemical disinfectants such as chlorine.

People acquire infection with *C. parvum* through drinking or unintentionally swallowing (such as when swimming) contaminated water. The parasites may also be present in foods rinsed or prepared with contaminated water. The INCUBATION PERIOD is 2 to 10 days and the illness lasts about 2 weeks. During the incubation period and when symptoms are present, the infection is contagious and the person may pass it to others. Proper HAND WASHING and other PERSONAL HYGIENE measures are essential to reduce this risk.

The primary symptom of cryptosporidiosis is profuse, watery DIARRHEA. In addition to the diarrhea, many people have abdominal cramping and low-grade FEVER. Treatment is supportive, emphasizing fluid replacement to prevent DEHYDRATION due to the diarrhea. People who are IMMUNOCOMPROMISED may require hospitalization for adequate fluid replacement and medical management of the diarrhea. Most otherwise healthy people fully recover after the infection runs its course.

See also AMEBIASIS; CYCLOSPORIASIS; DRINKING WATER STANDARDS; FOODBORNE ILLNESSES; GIARDIASIS; OPPORTUNISTIC INFECTION; WATERBORNE ILLNESSES.

cyclosporiasis An illness that results from INFECTION with the PARASITE *Cyclospora cayetanensis.* The *Cyclospora* come to maturity in warm, moist environments after excretion in the feces of people who have the infection. This parasite, unlike most, cannot cause immediate infection so people who are infected are not contagious. People acquire infection with *Cyclospora* through eating foods or drinking water contaminated with the parasites. The *Cyclospora* infect the SMALL INTESTINE, causing abdominal cramping and watery DIARRHEA. Some people also have low-grade FEVER and generalized discomfort.

The incubation period (time from infection to illness) is five to seven days. Diagnosis is through laboratory examination of stool samples, which reveals the *Cyclospora* cysts. Treatment is a course of therapy with ANTIBIOTIC MEDICATIONS, usually the combination antibiotic drug trimethoprim-sulfamethoxazole (TMP-SMZ), along with diligent rehydration. Most people recover rapidly and completely with treatment. Without treatment, relapses of symptoms are common and can continue over a period of several months before full recovery occurs.

See also COCCIDIOIDOMYCOSIS; CRYPTOCOCCOSIS; CRYPTOSPORIDIOSIS; FOODBORNE ILLNESSES; FOOD SAFETY; OPPORTUNISTIC INFECTION; WATERBORNE ILLNESSES.

cytomegalovirus (CMV) A member of the herpesvirus family, also called human herpesvirus-5 (HHV-5). Like other herpesviruses, CMV is ubiquitous throughout the world—85 percent of Americans have CMV INFECTION by age 40. However, CMV infection primarily causes illness only in people who are IMMUNOCOMPROMISED, such as people who have HIV/AIDS or who take long-term IMMUNOSUPPRESSIVE THERAPY after ORGAN TRANSPLANTATION. CMV is also a significant risk for the unborn child of a woman whose initial infection with the VIRUS occurs during PREGNANCY. CMV virus crosses the PLACENTA to the fetus, causing congenital CMV infection. Most infants are born unharmed; however, CMV infection can affect hearing, vision, and intellectual capacity.

When CMV infection causes illness, symptoms typically include NAUSEA, VOMITING, DIARRHEA, JAUNDICE, and FEVER. The person often has an enlarged and tender LIVER (HEPATOMEGALY) and SPLEEN (SPLENOMEGALY). Doctors may suspect infectious mononucleosis or HEPATITIS, though tests for these conditions come back negative. A BLOOD test can

detect the presence of CMV antibodies to confirm the diagnosis of CMV infection. Though most people recover without complications, CMV infection can be serious or fatal in people who are immunocompromised. ANTIVIRAL MEDICATIONS are not very effective in treating the infection; treatment primarily targets symptoms.

See also ANTIBODY; EPSTEIN-BARR VIRUS; HERPES SIMPLEX; HERPES ZOSTER; MONONUCLEOSIS, INFECTIOUS; OPPORTUNISTIC INFECTION.

D–E

diphtheria An illness that results from INFECTION with the bacterium *Corynebacterium diphtheriae*. Routine childhood IMMUNIZATION has made diphtheria rare in the United States, though the infection can occur in people who do not receive a booster VACCINE every 10 years and is common in other parts of the world.

Infection may involve the NOSE and THROAT (respiratory diphtheria) or the SKIN (cutaneous diphtheria). *C. diphtheriae* BACTERIA that infect the throat produce a toxin that causes a thick layer of cells and mucus to accumulate in the throat, forming a membrane that impairs BREATHING. Respiratory diphtheria is life threatening and requires urgent administration of diphtheria ANTITOXIN, which counters the toxin the *C. diphtheriae* bacteria produce, in combination with ANTIBIOTIC MEDICATIONS to kill the *C. diphtheriae* bacteria (typically erythromycin or penicillin G). Diphtheria that occurs in the United States is most often cutaneous. Cutaneous diphtheria causes painful, red sores on the skin. Antibiotic therapy is often adequate to treat the infection, though sometimes doctors also administer diphtheria antitoxin.

The INCUBATION PERIOD for either type of diphtheria is two to five days after exposure. The infection is contagious for up to two weeks after symptoms emerge. The course of uncomplicated illness is four to six weeks. Respiratory diphtheria (especially when untreated) may result in complications that include MYOCARDITIS (INFLAMMATION and infection of the HEART MUSCLE), NEURITIS, RESPIRATORY FAILURE, and death. Childhood immunization with booster vaccines every 10 years is the most effective means of prevention. Some people are carriers of *C. diphtheriae* bacteria, which requires human hosts for survival. Carriers have the infection present in their bodies but do not become ill, though they can pass the infection to others. ANTIBIOTIC PROPHYLAXIS prevents infection in people who are exposed to *C. diphtheriae*.

See also CHILDHOOD DISEASES; PREVENTIVE HEALTH CARE AND IMMUNIZATION.

encephalitis INFLAMMATION and INFECTION of the BRAIN. Encephalitis usually results from infection with a VIRUS and is potentially life threatening. Infection can enter the brain via pathogens that are small enough to pass across the BLOOD–BRAIN BARRIER or that are able to follow neural pathways (the routes of nerves) into the brain. The most common cause of encephalitis is infection with an arbovirus transmitted through the bite of a mosquito or tick. Other viruses that typically cause common infections may affect the brain to cause encephalitis, and encephalitis may develop as a complication of viral infection (and less commonly bacterial infection) elsewhere in the body. TOXOPLASMOSIS, a parasitic infection, may also cause encephalitis.

VIRUSES THAT CAN CAUSE ENCEPHALITIS

CYTOMEGALOVIRUS (CMV)	California VIRUS
eastern equine virus	EPSTEIN-BARR VIRUS
HERPES SIMPLEX virus (HSV)	LaCrosse virus
MUMPS virus	Powassan virus
RUBELLA virus	rubeola (MEASLES) virus
St. Louis virus	varicella zoster viruses
West Nile virus	western equine virus

Symptoms and Diagnostic Path

The symptoms of encephalitis differ somewhat in children and in adults. Children often become lethargic, confused, irritable, and sensitive to light;

older children may complain of severe HEADACHE. Adults often exhibit changes in mental alertness, cognitive ability, and emotional stability and may have severe headache. Both children and adults may have seizures, FEVER, NAUSEA, and VOMITING.

Diminished awareness or loss of consciousness that accompanies or follows other symptoms of encephalitis is an indication of serious INFECTION that requires urgent medical attention.

The diagnostic path includes LUMBAR PUNCTURE to determine the presence of pathogens or white BLOOD cells, or excessive fluid or increased pressure in the spinal column, any of which may indicate infection. Blood tests may show the presence of certain viruses. Diagnostic procedures such as electroencephalogram (EEG) and COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) can show abnormalities of brain function and structure that are characteristic of encephalitis.

Treatment Options and Outlook

Mild viral encephalitis generally runs its course within five to seven days and does not require treatment beyond ANALGESIC MEDICATIONS such as acetaminophen to relieve fever and headache. ANTIVIRAL MEDICATIONS can reduce the severity of symptoms and length of illness for some forms of viral encephalitis, notably those resulting from viruses in the herpes family, though have no effect against encephalitis resulting from arboviruses. CORTICOSTEROID MEDICATIONS to suppress the inflammatory response can reduce intracranial swelling and pressure that commonly accompanies encephalitis. Bacterial encephalitis, which is much less common than viral encephalitis and usually a secondary infection, requires treatment with antibiotic medications. Antibiotics are not effective against viral infections.

Recovery depends on the severity of symptoms and the causative PATHOGEN. Though viral encephalitis is generally more mild than bacterial encephalitis, it can be fatal, particularly in infants, the very elderly, and people who are IMMUNOCOMPROMISED. People who have mild encephalitis recover completely and without residual complications. More severe illness may result in permanent brain damage and corresponding cognitive dysfunction, memory impairment, LEARNING DISORDERS, PARALYSIS, SEIZURE DISORDERS, or speech disorders.

Risk Factors and Preventive Measures

The risk for viral encephalitis is greatest during times of the year when mosquito and tick activity is highest, typically May through October in most parts of the United States. Other risks include living in close contact, such as in dormitories and institutions, and infection elsewhere in the body that migrates to the brain. Prevention efforts include public health measures to control mosquito populations and individual efforts to minimize exposure to mosquitoes and ticks.

See also COGNITIVE FUNCTION AND DYSFUNCTION; MEMORY AND MEMORY IMPAIRMENT; MENINGITIS.

Epstein-Barr virus A member of the herpesvirus family best known for causing the illness infectious mononucleosis. INFECTION with the Epstein-Barr VIRUS, also called human herpesvirus-4 (HHV-4), causes other disease as well and was the first virus researchers linked with cancer (notably Burkitt's lymphoma). Epstein-Barr virus is ubiquitous; it infects more than 90 percent of Americans by age 25.

As is characteristic of herpesvirus infections, Epstein-Barr virus causes first an acute illness (infectious mononucleosis), then retreats into a state of dormancy and remains in the body as a latent infection that does not cause illness or symptoms. B-cell lymphocytes, white BLOOD cells key to ANTIBODY-MEDIATED IMMUNITY, harbor the latent Epstein-Barr virus. Though the virus does not change the ability of its host B-cell lymphocytes to function within the IMMUNE RESPONSE, it does alter their DNA such that they become immortalized—they lose their genetic encoding for APOPTOSIS, the natural process for cell death.

Only a small percentage of B-cell lymphocytes contain the virus, so for the most part immune function continues as normal. A healthy IMMUNE SYSTEM maintains a balance between B-cell lymphocytes and T-cell lymphocytes (white blood cells key to CELL-MEDIATED IMMUNITY) that prevents B-

cell lymphocytes containing the latent Epstein-Barr virus from endlessly proliferating. As a result of this balance, in most people the virus never regains enough presence to again cause illness.

Circumstances that challenge the immune system allow the Epstein-Barr virus to reactivate. The most notable of these circumstances are HIV/AIDS and IMMUNOSUPPRESSIVE THERAPY after ORGAN TRANSPLANTATION. The reactivated Epstein-Barr virus may cause symptoms similar to infectious mononucleosis (chronic infectious mononucleosis) during which the person may spread the virus to others. It may also cause lymphoproliferative disorders: abnormal growth (tumors) of lymphatic structures such as lymph nodes and MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT). Though research is under way to develop a VACCINE to prevent infection with Epstein-Barr virus, at present there are no effective measures to prevent infection with the virus and no treatments to eradicate the virus once it establishes infection.

DISEASES ASSOCIATED WITH EPSTEIN-BARR VIRUS

acute infectious mononucleosis	AIDS-associated lymphoma
chronic infectious mononucleosis	Burkitt's lymphoma
nasopharyngeal CARCINOMA	generalized lymphoproliferative disease
	post-transplant lymphoproliferative disorder (PTLD)

See also B-CELL LYMPHOCYTE; CELL STRUCTURE AND FUNCTION; HERPES SIMPLEX; HERPES ZOSTER; KAPOSI'S SARCOMA; LYMPH NODE; LYMPHOCYTE; MONONUCLEOSIS, INFECTIOUS; OPPORTUNISTIC INFECTION; T-CELL LYMPHOCYTE.

***Escherichia coli* infection** Illness that results from INFECTION with any of the numerous strains of *Escherichia coli* BACTERIA, some of which are NORMAL FLORA in the human gastrointestinal tract and others that are normal flora in the gastrointestinal tracts of animals consumed as food (such as cattle and poultry). Most strains of *E. coli* cause mild to moderate illness. Illness from *E. coli* infection results from the toxins the *E. coli* release through their normal metabolic functions. The strain *E. coli* O157:H7, found in beef contaminated with fecal matter, can cause particularly severe illness.

Symptoms and Diagnostic Path

The symptoms of common *E. coli* infection are generally mild to moderate in severity and include

- abdominal cramping
- DIARRHEA
- occasionally NAUSEA and VOMITING

The symptoms of *E. coli* O157:H7 infection are often more severe and include ABDOMINAL PAIN with profuse, sometimes bloody diarrhea. Though most people recover fully after the illness runs its course in 5 to 10 days, in some people the toxins the *E. coli* O157:H7 release cause the massive destruction of red BLOOD cells (erythrocytes), a process called HEMOLYSIS. The enormous volume of dead erythrocytes creates proteins in the blood that are damaging to the KIDNEYS, resulting in RENAL FAILURE. The combination of these circumstances is HEMOLYTIC UREMIC SYNDROME (HUS), which occurs as a complication of *E. coli* O157:H7 infection in about 5 percent of people (mostly children under age 5). HUS nearly always results in END-STAGE RENAL DISEASE (ESRD), requiring dialysis or KIDNEY TRANSPLANTATION.

The diagnostic path for *E. coli* infection may include culture of stool samples to determine the causative PATHOGEN, though most often doctors do this only when the illness continues beyond about two weeks or has severe symptoms. The doctor must specifically request culture for *E. coli* O157:H7 as most laboratories do not routinely include this in their testing.

Treatment Options and Outlook

E. coli diarrheal illnesses are very common and nearly all people who acquire them fully recover in three to five days without treatment, except fluid replacement to prevent DEHYDRATION. ANTIBIOTIC MEDICATIONS are seldom appropriate because the cause of symptoms is the toxins the *E. coli* bacteria release, and killing the bacteria causes them to release even more toxins. It is sometimes helpful to avoid dairy products until bowel activity returns to normal. People who become seriously ill with *E. coli* O157:H7 may require care in the hospital. Though *E. coli* O157:H7 infection has gained substantial notoriety, more than 95 percent

of people who become ill with it recover without complications.

Risk Factors and Preventive Measures

E. coli infections result from contaminated water or food, especially meats. Swimming in lakes and rivers often exposes people to *E. coli* contamination; swallowing the water allows the bacteria to enter the gastrointestinal system. Most *E. coli* infections are FOODBORNE ILLNESSES.

Preventive measures include

- diligent HAND WASHING
- following FOOD SAFETY guidelines for handling and preparing meats and other foods
- thoroughly cooking meats, especially ground beef

Most *E. coli* infections are preventable.

See also ERYTHROCYTE; WATERBORNE ILLNESSES.

F–G

fever An elevation of body temperature above the normal range. Body temperature varies over the course of a circadian cycle, roughly equivalent to 24 hours, to accommodate the body's metabolic needs. Body temperature is lowest just before waking in the morning and highest in the late afternoon or early evening, times that typically correlate with the body's lowest and highest expenditures of energy. The normal range of body temperature is 97.6°F to 99.6°F, with the mean of 98.6°F generally perceived as the standard normal temperature. Health-care providers generally view a body temperature of 100°F or higher as a fever.

The body's IMMUNE RESPONSE raises body temperature as a mechanism for fighting INFECTION. Elevated body temperature increases the body's METABOLISM, which enhances the IMMUNE SYSTEM's ability to contain and eradicate the pathogens responsible for infection. Each degree of elevation in body temperature accelerates metabolism by 10 to 15 percent. The various types of white BLOOD cells (leukocytes) release INTERLEUKINS, PROSTAGLANDINS, TUMOR NECROSIS FACTORS (TNFS), and other biochemicals (CHEMOKINES) that temporarily reset the body's thermoregulatory mechanisms.

Though common practice is to attempt to lower a fever through measures such as cool baths and acetaminophen or other medications, doctors now believe fever does not ordinarily require treatment. To the contrary, recent research shows that the immune response and most ANTIBIOTIC MEDICATIONS work more effectively when body temperature is elevated. Doctors recommend treating fever only when there is risk for febrile seizures, when the person cannot eat or drink enough to meet the body's metabolic needs, or when the fever creates discomfort. Medications to treat other symptoms due to the infection, such as HEADACHE, also reduce fever.

See also ANALGESIC MEDICATIONS; HEAT EXHAUSTION; HEAT STROKE; LEUKOCYTE; NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS); PATHOGEN.

foodborne illnesses Diseases resulting from consumption of foods contaminated with pathogenic BACTERIA, fungi, parasites, or viruses. Foodborne illnesses, also called food poisoning, are common, affecting 76 million Americans each year. There are several hundred known foodborne illnesses, most of which cause mild to moderate gastrointestinal symptoms including abdominal cramping, NAUSEA, VOMITING, and DIARRHEA. Illness results from consuming a food contaminated with pathogens. Common sources include undercooked meats and cooked foods that remain at room temperature for longer than two hours. Most often, it is not possible to tell from taste, smell, or appearance that a food contains pathogens.

Prevention is the primary focus when it comes to foodborne illnesses. The simple measure of washing the hands before and after preparing foods, eating meals, changing diapers, and using the bathroom could eliminate many foodborne illnesses by preventing bacteria and other pathogens from contact with foods. Other FOOD SAFETY measures to reduce the risk for infection from foodborne pathogens include

- using separate utensils and surfaces for meats and for other foods
- washing fruits and vegetables, including "rind" fruits such as oranges and watermelon, in running water before eating or preparing them

- thoroughly cooking all animal-based foods (including eggs), to 160ºF for most meats and poultry (no pink in the flesh)
- prompt refrigeration of leftover foods

Most foodborne illnesses are self-limiting; the infection runs its course (usually within three to five days) and the person fully recovers without medical treatment. Supportive treatment such as adequate fluid intake is important to prevent DEHYDRATION; soups and juices also help maintain nutrition. Doctors often discourage people from taking ANTIDIARRHEAL MEDICATIONS that work by slowing gastrointestinal motility, such as loperamide or diphenoxylate, because these drugs may prolong the illness by prolonging the presence of the PATHOGEN in the gastrointestinal tract.

Some foodborne illnesses need prompt medical treatment, such as BOTULISM. Some parasitic and bacterial infections require appropriate medications. Some foodborne illnesses may spread from one person to another, such as HEPATITIS and *ESCHERICHIA COLI* INFECTION. A doctor should evaluate symptoms that are severe or persist longer than five days.

FOODBORNE ILLNESSES

AMEBIASIS	BOTULISM
CAMPYLOBACTERIOSIS	*Escherichia coli* INFECTION
GIARDIASIS	HEPATITIS
LISTERIOSIS	Norwalk-like virus
SALMONELLOSIS	SHIGELLOSIS
TOXOPLASMOSIS	

See also FUNGUS; PARASITE; VIRUS; WATERBORNE ILLNESSES.

fungus Any of the 200,000 or so of single or multiple cell organisms (living structures), microscopic (visible only using a microscope for magnification) and macroscopic (visible to the unaided EYE), that are abundant in the natural environment. Yeasts are single-cell fungi that live in colonies; molds are multiple-cell fungi that form structures. Like BACTERIA, fungi are among the oldest life forms to inhabit the Earth; fossils of yeasts date back more than 2 billion years.

Most fungi are harmless to humans and many are NORMAL FLORA (present in body and on the SKIN). Fungi break down organic waste; yeasts, for example, populate the gastrointestinal tract where they aid in digestion. Many ANTIBIOTIC MEDICATIONS derive from fungi, notably penicillin (first cultivated from the mold *Penicillium chrysogenum*).

Some fungi are pathogenic (disease causing) in people under any circumstances and others cause OPPORTUNISTIC INFECTION in people who are IMMUNOCOMPROMISED. Fungal diseases may be localized, such as ONYCHOMYCOSIS (fungal INFECTION of the nail beds), or systemic, such as HISTOPLASMOSIS. Doctors use ANTIFUNGAL MEDICATIONS to treat fungal infections that cause disease.

FUNGAL DISEASES

ASPERGILLOSIS	blastomycosis
CANDIDIASIS	COCCIDIOIDOMYCOSIS
CRYPTOCOCCOSIS	HISTOPLASMOSIS
mucormycosis	ONYCHOMYCOSIS
sporotrichosis	tinea barbae (ringworm)
tinea capitis (ringworm)	tinea corporis (ringworm)
tinea cruris (jock itch)	tinea pedis (athlete's foot)

Fungi may also be a source of poisoning. *Aspergillus* molds on grains produce aflatoxins, for example, which cause LIVER damage and are associated with LIVER CANCER. Many types of mushrooms produce toxins (mycotoxins) that cause illness or death when eaten, such as the highly toxic "death cap" mushroom, *Amanita phalloides*. Molds may grow in buildings where humidity and darkness converge to provide the ideal environment for their growth, such as inside walls and floors where there have been water leaks. The spores of these fungi cause respiratory illnesses and other health problems when breathed in with the air, particularly for people who have ASTHMA or other chronic pulmonary conditions.

See also BUILDING-RELATED ILLNESS; INDOOR AIR QUALITY; MICROBE; OCCUPATIONAL HEALTH AND SAFETY; PARASITE; PATHOGEN; PROTOZOA; TINEA INFECTIONS; VIRUS.

genital herpes A sexually transmitted disease (STD) resulting from INFECTION with herpesvirus, usually HERPES SIMPLEX VIRUS 2 (HSV-2). Herpes

simplex virus 1 (HSV-1), which causes cold sores, may also cause sores in the genital area. Genital herpes is one of the most prevalent STDs in the United States, infecting about 25 percent of teens and adults—more than 45 million people. About 1 million new infections occur each year.

As is characteristic of the herpesviruses, HSV-2 remains in the body for life after the initial infection, retreating to NERVE roots within the areas of infection. Periodically the virus travels along the nerves to the surface of the SKIN, causing outbreaks of blisters that become crusted sores. During these outbreaks the virus both replicates and sheds, and the infected person is highly contagious. Such a pattern of REMISSION and RECURRENCE continues through life; there currently is no cure for genital herpes.

Direct contact with SEMEN, vaginal fluids, and saliva spreads genital herpes from one person to another during vaginal intercourse, anal intercourse, or oral sex. The infection does not spread via contact with objects such as toilet seats or in water (such as swimming pools and hot tubs). Genital herpes is contagious even when no sores are present. Because symptoms may be mild, or in women occur within the VAGINA, many people do not know they have genital herpes. The first outbreak of symptoms tends to be the most severe. Over time outbreaks tend to become less frequent with fewer and smaller sores.

Symptoms and Diagnostic Path

Symptoms, when they occur, begin about two weeks after sexual contact with an infected person who is shedding the virus. Initial symptoms may include

- tingling, burning, or pain at the site of infection (PENIS, vagina, CERVIX, ANUS, RECTUM, MOUTH, and sometimes on skin surfaces)
- FEVER
- HEADACHE
- swollen LYMPH nodes near the site of the infection
- vaginal discharge in women
- painful URINATION in men

The hallmark symptom of genital herpes is painful sores that begin as red bumps that BLISTER and then crust. The sores appear at the sites where the virus entered the body and are usually most severe with the first outbreak. Symptoms of subsequent outbreaks tend to be more mild, though sores may appear in new locations as the virus spreads along nerve paths. The sores are present for three to four weeks and then heal without scarring. Periods of remission during which there are no sores or other symptoms may last several weeks to several months.

Health-care providers generally presume a diagnosis of genital herpes when the characteristic sores are present in a person who is sexually active. BLOOD tests can detect the presence of HSV antibodies but this is not especially useful information from a diagnostic perspective because more than 90 percent of people have some sort of herpesvirus infection—herpes simplex, HERPES ZOSTER, varicella (CHICKENPOX)—that activates the ANTIBODY response and blood tests cannot distinguish among the type of herpesvirus present. Cultures of the sores may produce HSV-2, which confirms the diagnosis. However, cultures of the sores may sometimes be negative even when HSV-2 infection is present.

Treatment Options and Outlook

The sores that erupt during a genital herpes outbreak will heal without treatment within two or three weeks. ANTIVIRAL MEDICATIONS can shorten the length of the outbreak and reduce the number and severity of the sores. Some people benefit from taking an antiviral medication daily, which may lessen the frequency of outbreaks. Valacyclovir is the medication doctors most commonly prescribe for regular use. Antiviral medications do not cure genital herpes, however.

ANTIVIRAL MEDICATIONS TO TREAT GENITAL HERPES

acyclovir	famciclovir	valacyclovir

Most people who have genital herpes experience outbreaks of symptoms several times a year. Stress, MENSTRUATION, and other viral infections such as COLDS seem to trigger outbreaks though symptoms may erupt without apparent cause. The open sores of genital herpes create increased risk for infection with HIV. A pregnant woman can pass genital herpes to her unborn child; doctors

may recommend CESAREAN SECTION (surgical delivery) for women whose infections are active (symptomatic) near the time of delivery to prevent this.

Risk Factors and Preventive Measures

Because HSV-2 infection is so prevalent, all sexually active people are at risk for genital herpes. Uninfected people who are in monogamous relationships with uninfected sexual partners have the lowest risk for infection; uninfected people who have multiple sexual partners or who are in relationships with sexual partners who have genital herpes have the highest risk for infection. At present the most effective means of prevention among sexually active adults is abstinence during outbreaks and barrier protection such as latex condoms during all sexual activity. Barrier protection is not absolute, however, as the HSV-2 virus may infect nerve cells at the skin's surface that the condom does not cover.

The antiviral medication valacyclovir significantly reduces viral shedding, slowing but not entirely preventing transmission of genital herpes. This preventive measure is most effective in monogamous relationships in which one person has HSV-2 and the other does not. Clinical studies are under way to evaluate a vaccine for genital herpes.

See also CHLAMYDIA; COLD SORE; CONTRACEPTION; GONORRHEA; HUMAN PAPILLOMAVIRUS (HPV); LYMPH NODE; OCULAR HERPES; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SEXUALLY TRANSMITTED DISEASES (STDS); SYPHILIS.

giardiasis An illness resulting from INFECTION with the protozoan *Giardia lamblia* (also called *Giardia intestinalis*). *Giardia* are abundant in fresh water throughout the United States; infection occurs through drinking contaminated water. The PROTOZOA infect the SMALL INTESTINE of humans and animals and can survive for extended periods without a host. The most common means of infection is through swallowing water in recreational settings, such as lakes, rivers, and streams. Fountains, swimming pools, and hot tubs that lack proper chlorination also may harbor *Giardia*. Giardiasis also spreads through fecal contamination by direct contact, such as by changing diapers, and can occur as a FOODBORNE ILLNESS spread through poor FOOD SAFETY practices.

Symptoms develop after an incubation period of 7 to 10 days and include DIARRHEA, excessive FLATULENCE (gas), abdominal discomfort, and NAUSEA. The diarrhea is watery and has a greasy appearance. Some people also experience fatigue, loss of APPETITE, and rapid weight loss. It is also possible to have giardiasis and have no symptoms. Stool samples examined under the microscope typically contain both cysts and trophozoites, the immature and mature forms, respectively, of the *Giardia*. Treatment is ANTIBIOTIC MEDICATIONS and ANTIFUNGAL MEDICATIONS. The course of illness runs four to six weeks with treatment, after which most people recover without complications or residual consequences. Without treatment giardiasis may persist for six to eight weeks, with gradual though complete recovery.

MEDICATIONS TO TREAT GIARDIASIS

albendazole	furazolidone
metronidazole	nitazoxanide
paromomycin	tinidazole

See also AMEBIASIS; BABESIOSIS; DRINKING WATER STANDARDS.

gonorrhea A sexually transmitted disease (STD) resulting from INFECTION with the bacterium *Neisseria gonorrhoeae*. *N. gonorrhoeae* infects 350,000 Americans each year, though public health officials believe another 350,000 people have gonorrhea that goes undiagnosed because they do not know they are infected. Gonorrhea is highly contagious and passes among sexual partners through vaginal intercourse, anal intercourse, or oral sex. People who have multiple sex partners have increased risk for gonorrhea as well as other STDs. Gonorrhea is a public health concern of great magnitude worldwide because a number of strains of *N. gonorrhoeae* have become resistant to the ANTIBIOTIC MEDICATIONS used to treat the infection.

Symptoms and Diagnostic Path

Gonorrhea has a 2- to 10-day INCUBATION PERIOD (time from exposure to symptoms) though often causes no symptoms, especially in women. Symptoms that do occur tend to be generalized and

vague, such as lower abdominal discomfort, and go away in a few days to a week. When symptoms are present they typically include

- a thick, discolored (yellowish or greenish), or bloody discharge from the PENIS in men and the VAGINA in women
- burning or PAIN with URINATION (more common in men)
- pain or bleeding during SEXUAL INTERCOURSE (more common in women)

Early symptoms will go away without treatment, though the infection remains. As the *N. gonorrhoeae* BACTERIA multiply in the body, they cause increasing irritation to the tissues, resulting in INFLAMMATION and the formation of SCAR tissue. In men the next level of infection with untreated gonorrhea is EPIDIDYMITIS, which causes swelling and pain in the TESTICLES, and URETHRITIS, which causes intense pain with urination. In women the next level of infection with untreated gonorrhea is PELVIC INFLAMMATORY DISEASE (PID), which involves the UTERUS and FALLOPIAN TUBES. PID often causes severe ABDOMINAL PAIN. Scarring from the infection blocks the fallopian tubes, putting a woman at high risk for ECTOPIC PREGNANCY.

Diagnosis is laboratory examination of a sample of the discharge taken from the penis (men) or the CERVIX (women). A fast test done in the doctor's office is highly accurate for men but not for women; for women, a conventional culture is the most reliable diagnostic procedure. The doctor likely will conduct diagnostic tests for other STDs as well, notably CHLAMYDIA and SYPHILIS. All sex partners should also undergo testing and receive treatment if they have gonorrhea, even if they do not have symptoms.

Treatment Options and Outlook

The current standard of treatment for gonorrhea is a single DOSE of a fluoroquinolone antibiotic, which cures the infection in most people. However, new strains of *N. gonorrhoeae* are showing resistance to these antibiotics, causing doctors to look to combinations of antibiotics and to stronger antibiotics to cure the infection.

ANTIBIOTIC MEDICATIONS TO TREAT GONORRHEA

azithromycin	cefixime
ceftriaxone	ciprofloxacin
levofloxacin	ofloxacin

The debut of penicillin in the 1940s provided the first cure for gonorrhea. However, 30 years later, most strains of *N. gonorrhoeae* were resistant to penicillin and to tetracycline, the second-choice antibiotic. Doctors can no longer prescribe these antibiotics to treat gonorrhea. Though antibiotic medications remain the standard of treatment for gonorrhea, doctors and public health officials worry that the ability of *N. gonorrhoeae* to adapt will soon put gonorrhea out of reach for treatment. Researchers have recently unraveled the GENETIC CODE (DNA sequence) of the *N. gonorrhoeae* and are hopeful this advance will lead to new kinds of treatments.

Risk Factors and Preventive Measures

Those who are at highest risk for gonorrhea and other STDs are

- women between the ages of 15 and 19
- men between the ages of 20 and 24
- men who have sex with men
- men or women who have multiple sex partners

Monogamy (having only one sex partner) and consistent use of latex condoms are measures that can prevent *N. gonorrhoeae* infection. People who are sexually active should undergo regular testing for STDs. Reinfection can occur.

See also ANTIBIOTIC RESISTANCE; GENITAL HERPES; HIV/AIDS; HUMAN PAPILLOMAVIRUS (HPV); SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SEXUALLY TRANSMITTED DISEASES (STDS).

hantavirus pulmonary syndrome An illness resulting from INFECTION with hantavirus. Certain species of deer mice carry the hantavirus, which they shed in their droppings, URINE, and saliva. People who come into contact with these excretions, which may be through direct touch or inhalation, may then acquire infection with the VIRUS. Deer mice live primarily in wooded areas. Most often a person acquires the infection after cleaning in barns and outbuildings where mouse droppings can accumulate; the cleaning stirs up dust that carries the virus into the respiratory tract. People who go camping in areas where there are large populations of deer mice also are at risk for infection.

The INCUBATION PERIOD (time between exposure and illness) is one to three weeks. Symptoms emerge abruptly and include FEVER, severe MUSCLE aches (particularly in the large muscles of the legs and back), and shortness of breath (DYSPNEA) that rapidly progresses to respiratory failure. A BLOOD test can show the presence of antibodies to confirm the diagnosis. Treatment is hospitalization, usually in an intensive care unit, to provide support for BREATHING while the virus runs its course. Hantavirus pulmonary syndrome is a very serious infection with a high fatality rate. Early, aggressive medical support offers the best potential for successful recovery.

See also ANTIBODY; HEMORRHAGIC FEVERS; MECHANICAL VENTILATION.

hemorrhagic fevers Life-threatening illness resulting from INFECTION with various viruses, spread by the bites of mosquitoes and ticks, the hallmark of which is the collapse of multiple organ systems because damage to the BLOOD vessels impairs their ability to contain and transport blood. The dozen or so viruses that cause hemorrhagic fevers belong to four viral families: arenaviruses, bunyaviruses, filoviruses, and flaviviruses. These viral families also contain viruses that cause infection other than hemorrhagic FEVER. For example HANTAVIRUS belongs to the bunyavirus family and the yellow fever VIRUS belongs to the flavivirus family. Viral hemorrhagic fever infections occur in tropical regions, notably Africa and South America.

HEMORRHAGIC FEVER VIRUSES

Arenaviruses	
Guanarito VIRUS	Junin virus
Lassa virus	Machupo virus
Sabia virus	
Bunyaviruses	
Crimean-Congo virus	Rift Valley virus
Filoviruses	
Ebola virus	Marburg virus
Flaviviruses	
Dengue virus	Omsk virus

Rodents, primarily certain species of rats and mice, harbor the viruses. Mosquitoes and ticks that feed on the rodents continue to spread the virus among rodent populations. Rodent droppings and other excretions, such as saliva and URINE, contain the viruses. The viruses can then infect people who come into contact with the excretions. Contact with body fluids from an infected person further spread the virus. Symptoms of illness arise suddenly and are severe, typically including high fever, fatigue, evidence of internal bleeding, and weakness. Subsequent

symptoms develop as organs fail. The only treatment for viral hemorrhagic fevers is supportive; the illnesses are usually fatal. Outbreaks of viral hemorrhagic fevers occur periodically. Global efforts are under way to find medical treatments that can halt the course of disease as well as to contain rodent, mosquito, and tick populations.

See also COMMUNITY SANITATION.

herpes simplex INFECTION with the herpes simplex VIRUS 1 (HSV-1) or HSV-2. HSV-1 primarily causes cold sores on the lips and in the MOUTH, transmitted through saliva. HSV-2 primarily causes GENITAL HERPES, a sexually transmitted disease (STD) that causes ulcerative sores on the genitals. However, either form of the virus can cause infection anywhere in the body. HSV-1 and HSV-2, like other herpes viruses, are highly contagious through contact with the sores and may also spread from one person to another even when no sores are present. Herpes simplex infection is lifelong, though symptoms characteristically wax and wane. About 90 percent of Americans have HSV-1 and about 30 percent have HSV-2.

The typical course of an outbreak begins with itching or tingling, called the prodrome, which gives way to the eruption of a BLISTER within 48 hours. Cold sores typically form as single blisters though may occur as multiple blisters in several locations; genital herpes sores tend to erupt in clusters. After two or three days the blisters rupture and form crusted sores that subsequently heal. The cycle from prodrome to HEALING lasts about 10 days. Because the course of illness is so characteristic, the doctor can usually make the diagnosis on the appearance of the sores. Laboratory culture of the fluid within a blister or sore can provide a definitive diagnosis.

After an outbreak of symptoms the virus retreats to the local NERVE roots where it remains dormant until the next outbreak. Researchers are not certain what factors initiate outbreaks though stress and exposure to sunlight appear to play key roles. Doctors sometimes prescribe ANTIVIRAL MEDICATIONS such as acyclovir for people who have six or more outbreaks of herpes simplex infection in a year or who have severe symptoms during outbreaks. Herpes infections may involve the eyes or the BRAIN, where they can cause permanent damage.

See also CANKER SORE; CHICKENPOX; COLD SORE; HERPES ZOSTER; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SEXUALLY TRANSMITTED DISEASES (STDS).

herpes zoster An INFECTION that results from reactivation of the varicella-zoster VIRUS, which lies dormant in the spinal NERVE roots after causing CHICKENPOX. The virus can remain dormant for decades; doctors do not know what reactivates it though suspect a combination of aging and stress to the IMMUNE SYSTEM. The infection travels the tract of a spinal nerve to the SKIN, causing burning or PAIN as it makes its way to the body's surface. Called the prodrome, this discomfort yields in about two days to a rash of painful blisters that erupts along the nerve's pathway, called a DERMATOME. The blisters rupture in three to five days and crusted sores form at the sites of the blisters.

Herpes zoster, also called shingles, occurs only on one side of the body, most commonly on the chest though may affect dermatomes anywhere on the body. The blisters of the herpes zoster outbreak can spread the virus, which can cause chickenpox in people who have not had it or have not received the varicella VACCINE. An uncomplicated outbreak of herpes zoster runs its course in three to four weeks, after which the virus again goes dormant. Treatment with an antiviral medication taken at the onset of pain but before blisters emerge (the prodrome) can significantly shorten the course of illness and decrease the severity of symptoms.

ANTIVIRAL MEDICATIONS TO TREAT HERPES ZOSTER

acyclovir	desciclovir
famciclovir	penciclovir
valacyclovir	

Complications after the outbreak abates may include damage to the eyes, loss of taste, and partial PARALYSIS of the face when the outbreak involves the trigeminal nerve. Post-herpetic NEURALGIA is pain that persists along the dermatome after the sores have completely healed, and may be debilitating. Unlike its predecessor infection, chickenpox, herpes zoster can recur though usually does not.

See also AGING, EFFECTS ON IMMUNE RESPONSE; BLISTER; GENITAL HERPES; HERPES SIMPLEX; SPINAL NERVES.

histoplasmosis An illness resulting from INFECTION with the FUNGUS *Histoplasma capsulatum*. This fungus, commonly called a mold, thrives in soils where bird droppings are abundant, such as chicken farms, barns where pigeons and starlings nest, and caves where bats roost. Histoplasmosis is endemic (continuously present) in the river valley areas of the central United States, where the rich and acidic soil provides an especially supportive environment for fungi to grow.

When inhaled, the *H. capsulatum* spores cause lesions in the LUNGS. An acute infection causes symptoms only in about 10 percent of people, though nonetheless can do considerable damage to lung tissue. Permanent scarring (granulomas and cavitations) often occurs in untreated histoplasmosis. Chronic histoplasmosis may develop in people who have underlying pulmonary disease or repeated exposure to *H. capsulatum* spores. The most significant risk of histoplasmosis is disseminated disease, in which the spores enter the BLOOD circulation and migrate to other organs throughout the body. Disseminated histoplasmosis, often an OPPORTUNISTIC INFECTION in people who have HIV/AIDS or are otherwise IMMUNOCOMPROMISED, has a high rate of fatality.

Symptoms and Diagnostic Path

Symptoms in acute histoplasmosis generally appear within two weeks of exposure and include

- FEVER
- HEADACHE
- JOINT PAIN
- MUSCLE aches
- nonproductive (dry) COUGH

People who inhale a large quantity of the spores may have extensive lung involvement that causes shortness of breath (DYSPNEA). The diagnostic path begins with a detailed personal health history with emphasis on exposure to bird droppings, blood tests, and a SKIN ANTIGEN test. Chest X-RAY reveals the characteristic histoplasmosis lesions, and may also show enlarged LYMPH nodes in the chest (hilar and mediastinal LYMPHADENOPATHY).

Treatment Options and Outlook

Acute histoplasmosis usually resolves without treatment, running a course much like that of a common upper respiratory infection. Bacterial PNEUMONIA may occur as a complication of acute histoplasmosis, requiring treatment with ANTIBIOTIC MEDICATIONS. Doctors prescribe ANTIFUNGAL MEDICATIONS to treat moderate to severe acute symptoms, chronic histoplasmosis, and disseminated histoplasmosis. With appropriate treatment, most people who have normal immunocompetence recover though residual lung damage is possible. Chronic and disseminated forms of infection often require long-term or lifelong treatment with antifungal medications.

ANTIFUNGAL MEDICATIONS TO TREAT HISTOPLASMOSIS

amphotericin B	itraconazole	ketoconazole

Risk Factors and Preventive Measures

People who work with live poultry or in outdoor areas that have large bird populations have increased risk for infection with *H. capsulatum*. Minimizing disturbance of the soil helps reduce the release of spores into the air. People who work in areas where exposure is a risk should wear respirators. Recreational activities in areas where birds or bats are common may also be a risk for exposure.

See also HANTAVIRUS; LESION.

HIV/AIDS An INFECTION with the human immunodeficiency virus (HIV) that ultimately results in the illness acquired immunodeficiency syndrome (AIDS). Though new HIV/AIDS infections are on the decline in the United States and other industrialized nations, HIV/AIDS remains endemic on the African continent.

HIV/AIDS spreads through contact with body fluids such as occurs with sexual contact (vaginal intercourse, anal intercourse, and oral sex) or through shared needles among intravenous DRUG users. Though previously infection through transfused BLOOD or blood products was a key means of infection, screening for HIV antibodies in donated

blood supplies has significantly reduced this risk and infection through blood products is now uncommon.

Though there are numerous treatments for HIV/AIDS, there is no cure. HIV, the infection, nearly always progresses to AIDS, the illness, over the course of 5 to 20 years. Aggressive treatment can further manage the symptoms and complications of AIDS for years to sometimes decades. However, AIDS is ultimately fatal. AIDS does not itself cause death but instead so extensively damages the IMMUNE SYSTEM, the infection's target, that the body cannot protect itself from infections or conditions such as cancer, which become the causes of death.

The Virus: HIV

The human immunodeficiency virus, HIV, is a retrovirus that exists in two known types, HIV-1 and HIV-2. Each infects the body in the same way and etches the same pathway to AIDS. HIV-1 is predominant in North America and Europe; HIV-2 is predominant in Africa, Southeast Asia, and China. HIV enters the body by attaching itself to a type of T-CELL LYMPHOCYTE called a CD4 cell (helper T-cell). CD4 cells direct the immune system's response to infection and are integral to CELL-MEDIATED IMMUNITY. Once attached, the HIV virion, the essential structure of the VIRUS before it acquires a host cell, can infiltrate the cell without the immune system detecting its presence.

As a retrovirus, HIV uses reverse transcriptase, an enzyme, to instruct the CD4 cell's RNA to replicate the virus's RNA in place of the cell's DNA. The cell then supports and replicates the virus, releasing new virions to infect additional CD4 cells. The entire process is quite stealthy. Therapeutic interventions are not quite of comparable stealth, though are getting closer to the mark. For example, ANTIVIRAL MEDICATIONS called nucleoside analogs can interject themselves into the process of reverse transcription, with the result that the cell produces "blank" DNA that fails to replicate the virus.

The Illness: AIDS

The ultimate outcome, at present, of HIV infection is the collapse of the immune system. Eventually the number of CD4 cells under HIV control is significantly greater than the number of CD4 cells under control of the immune system. Critical mass shifts and the immune system becomes deficient: It lacks the resources to rally against even the most minor of infections. Illness ranging from CANDIDIASIS (yeast infection) to AIDS-related lymphoma (a type of cancer) takes over. It is these illnesses, not HIV/AIDS, that causes death.

Symptoms and Diagnostic Path

About two weeks after infection with HIV, mild flulike symptoms appear that last 10 to 14 days. Most people do not recognize these symptoms as HIV infection. After these initial symptoms resolve, there are no further symptoms until AIDS emerges. However, HIV antibodies become present in the body three to six months after infection (called seroconversion). Various tests are available to detect the presence of HIV antibodies, which confirm that a person has HIV infection (is HIV-positive). HIV infection is not the same as AIDS. AIDS is the end-stage outcome of HIV infection. At present the diagnostic criteria for the transition from HIV infection to AIDS is a CD4 count below 200 cells per cubic millimeter (mm^3) and/or the development of an AIDS-defining clinical conditions (an illness that a healthy immune system would block from occurring).

AIDS-DEFINING CLINICAL CONDITIONS

AIDS-associated lymphoma	Burkitt's lymphoma
CANDIDIASIS	chronic HERPES SIMPLEX
COCCIDIOIDOMYCOSIS	CRYPTOCOCCOSIS
CRYPTOSPORIDIOSIS	CYTOMEGALOVIRUS (CMV) disease or retinitis
HISTOPLASMOSIS	invasive CERVICAL CANCER
HIV-related ENCEPHALOPATHY	KAPOSI'S SARCOMA
isosporiasis	*Pneumocystis carinii* PNEUMONIA
Mycobacterium avium complex	*Salmonella* SEPTICEMIA, recurrent
progressive multifocal leukoencephalopathy	TUBERCULOSIS
TOXOPLASMOSIS of brain	
wasting syndrome due to HIV	

Treatment Options and Outlook

There are numerous treatment protocols for HIV/AIDS that extend both life expectancy and QUALITY OF LIFE. Early HIV infection does not require treatment beyond lifestyle measures to stay as healthy as possible. As the HIV begins to

compromise the immune system, aggressive treatment with a regimen called HAART (highly active antiretroviral therapy), which combines three or more medications taken daily, can delay the progression of infection. Three factors influence the decision to begin HAART:

- CD4 count (the number of CD4 T-lymphocytes in the blood circulation) below 350 cells per cubic millimeter (mm^3)
- viral load (the number of copies of HIV in the blood circulation) above 100,000 per milliliter (ml)
- presence of symptoms or an AIDS-defining clinical condition

Doctors wait to start HAART until these conditions exist because the antiretroviral drugs have potentially serious side effects, necessitating a careful balance between benefit and risk, and because once started, treatment is lifelong.

ANTIRETROVIRAL DRUGS TO TREAT HIV/AIDS (HAART)

Nonnucleoside Reverse Transcriptase Inhibitors (NNRTIs)		
delavirdine	efavirenz	nevirapine
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)		
abacavir	didanosine	emtricitabine
lamivudine	stavudine	tenofovir
zalcitabine	zidovudine	
Protease Inhibitors (PIs)		
amprenavir	atazanavir	fosamprenavir
indinavir	lopinavir	nelfinavir
ritonavir	saquinavir	tipranavir
Fusion Inhibitors		
enfuvirtide		

Regular blood tests to monitor CD4 counts and viral load determine how well a particular drug combination is working. Because drug toxicity and resistance are both problems with long-term HAART, it is sometimes necessary to change regimens.

Risk Factors and Preventive Measures

Numerous risk factors exist for HIV/AIDS. Key among them are

- unprotected vaginal intercourse, anal intercourse, or oral sex
- multiple sexual partners
- intravenous drug use with shared needles
- infection with SEXUALLY TRANSMITTED DISEASES (STDS) that have open sores, such as SYPHILIS and GENITAL HERPES
- vaginal intercourse during MENSTRUATION

Use of condoms with all sexual activity reduces the risk for spreading the virus but does entirely prevent infection. Pregnant women who are HIV-positive should discuss prophylactic treatment during PREGNANCY and for the infant after birth.

See also ANTIBODY; ANTIBODY-MEDIATED IMMUNITY; HIV/AIDS PREVENTION; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

human ehrlichiosis Any of several illnesses resulting from INFECTION with various species of *Ehrlichia* BACTERIA. Human ehrlichiosis infection spreads via tick bites. The tick species and the *Ehrlichia* species vary by geographic region. *Ehrlichia* bacteria infect white BLOOD cells. The two main forms of human ehrlichiosis in the United States are human granulocytic ehrlichiosis (hGE), in which the infection involves granulocytes (primarily neutrophils), and human monocytic ehrlichiosis (hME), in which the bacteria infect monocytes and macrophages. hME is about twice as common as hGE.

The INCUBATION PERIOD for human ehrlichiosis is 5 to 10 days, after which symptoms appear that are flulike in nature. Symptoms may include

- FEVER
- HEADACHE and general sense of not feeling well (malaise)
- JOINT PAIN and MUSCLE aches
- NAUSEA, VOMITING, and DIARRHEA

The diagnostic path includes blood tests to evaluate blood cell counts. The bacteria are also apparent with microscopic examination of a blood sample. *Ehrlichia* bacteria are highly sensitive to doxycycline, an antibiotic in the tetracycline family of ANTIBIOTIC MEDICATIONS. Because blood test results may take a week or longer, responsiveness

to antibiotic therapy is often a diagnostic measure. People who have human ehrlichiosis show marked improvement in symptoms within 24 to 36 hours of beginning doxycycline treatment. Most people recover fully with appropriate treatment. Though some people develop mild illness with few symptoms and fully recover without treatment, untreated human ehrlichiosis can become very serious very quickly because the attack on the white blood cells compromises immune function.

The risk for *Ehrlichia* infection in the United States is highest during the summer months (May through October) when people are hiking and camping in areas where ticks thrive. Measures to prevent tick bites include wearing protective clothing (such as long pants tucked into socks) or using an appropriate insect repellent and checking the SKIN carefully for ticks or signs of bites after being in wooded areas.

See also GRANULOCYTE; MACROPHAGE; MONOCYTE; ROCKY MOUNTAIN SPOTTED FEVER.

human papillomavirus (HPV) A family of more than 100 strains of VIRUS, various strains of which cause common WARTS, genital HPV infection, and CERVICAL CANCER.

HPV and Common Warts

The strains of HPV that cause common warts are mildly contagious and are more likely to spread to different locations on a person's body rather than to other people. These strains include

- HPV-2, HPV-4, and HPV-7, which cause the raised, rounded warts commonly found on the hands and fingers
- HPV-3 and HPV-7 cause flat, round warts that typically grow on the face and backs of the hands
- HPV-1, which causes plantar warts on the plantar surfaces, or soles, of the feet

Common warts typically do not cause symptoms other than their appearance, which people tend to find cosmetically displeasing. Numerous products and methods are available to remove them. Over time, most warts left on their own gradually recede and disappear as the IMMUNE SYSTEM dispenses with the virus that causes them. Plantar warts, because they are on the walking surface of the foot, often become painful. Plantar warts are also more commonly spread among people, typically via exposure in locker rooms and shower rooms where people walk barefoot.

Genital HPV Infection

Genital HPV INFECTION is the most common of the SEXUALLY TRANSMITTED DISEASES (STDS) in the United States, causing new infection in over 5 million people each year. More than 20 million people currently have HPV infections. More than 40 strains of HPV cause genital HPV infection. These strains are contagious among people and spread via sexual contact (vaginal intercourse, anal intercourse, and oral sex). Some strains produce no symptoms.

HPV-6 and HPV-11 produce fleshy growths, often called genital warts, at the sites where the virus enters the body. Commonly genital warts grow on the tip of the PENIS, on the VULVA and at the opening of the VAGINA, and around the ANUS. Genital warts may also grow within the vagina and on the CERVIX in women and on the SCROTUM in men. Genital HPV may infect the MOUTH and THROAT through oral sex, though this is much less common than genital infection.

Women may first learn they have genital HPV infection during a ROUTINE MEDICAL EXAMINATION when the health-care provider detects genital warts inside the vagina and on the cervix. The gynecologist may perform COLPOSCOPY, an examination of the interior vagina with a specialized microscope, for further diagnostic assessment and to remove tissue samples (biopsy). Genital warts turn white after a few minutes when dabbed with a mild acetic acid solution (vinegar), providing the doctor with a quick diagnostic assessment. Laboratory examination of tissue samples from the growths can confirm the diagnosis.

Because genital warts continue to grow, which both cultivates and sheds the virus, doctors recommend treatment to remove them. Treatment options include medications, cryosurgery (freezing), electrocautery (burning), and laser therapy. Genital warts tend to recur, however, as long as the HPV infection remains present in the body.

TOPICAL MEDICATIONS TO TREAT HPV GENITAL WARTS

bichloracetic acid (BCA)	5-fluorouracil cream
imiquimod cream	podofilox solution
podophyllin solution	trichloroacetic acid (TCA)

Most HPV strains that cause genital infection do not produce symptoms. Many of these asymptomatic infections are benign (harmless) and go away in two or three years. Other genital HPV infections cause molecular changes in the cells of tissues. The tissues most commonly affected are the walls of the vagina and the cervix. These changes, called DYSPLASIA, are detectable only through microscopic examination of cells such as the doctor collects for a routine PAP TEST. Though often dysplasia resolves over time without treatment, it may progress to cancer. Doctors generally treat dysplasia to remove the risk for such progression.

Genital HPV Infection and Cancer

In recent years researchers have discovered that nearly all primary cervical cancer tumors contain one or more of 13 strains of HPV. Further, primary cervical cancer rarely occurs in women who have never had HPV infection. Cancer experts now believe HPV infection is the cause of primary cervical cancer. HPV types 16, 18, 31, 33, 39, 45, 51, 52, 56, 58, 59, 68, and 69 are the causative strains; HPV-16 and HPV-18 together account for about 85 percent of cervical cancers. Though these strains of HPV cause cervical cancer, only a small percentage of women infected with them develop cervical cancer. Routine Pap tests are a woman's best defense against HPV infection leading to cervical cancer because the changes in cells takes place slowly over years. Detecting and treating cervical or vaginal dysplasia eliminates the risk for the cells to continue a transition to cancer.

Preventing HPV Infection

Because human papillomaviruses are so prevalent, avoiding infection is difficult. Minimizing touch with common warts and treating them while they are small reduces the risk for spreading them to other parts of the body. Wearing shower sandals in locker rooms and public showers reduces the risk for contracting HPV-1 infection, which causes plantar warts.

Because of the risk for infection with one of the HPV strains linked with cancer, prevention measures are particularly important for genital HPV infection. Using latex condoms during all sexual activity greatly reduces the likelihood of contact with genital warts as well as with infected tissues that do not show symptoms. Annual Pap tests are essential for sexually active women. Men and women who have multiple sex partners have increased risk for genital HPV infection.

In 2006 the US Food and Drug Adminstration (FDA) approved the first vaccine to prevent infection with HPV types 6, 11, 16, and 18 in women. Administered as three injectons over 6 months, the vaccine appears to be highly effective with minimal side effects. However, the vaccine does not benefit women who already have HPV infection. Health experts recommend women through age 26 receive the HPV vaccine and girls receive HPV vaccine at age 11 or 12.

See also CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN); CHLAMYDIA; GENITAL HERPES; GONORRHEA; HIV/AIDS; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SYPHILIS.

I

immunization The mechanism through which the body protects itself from subsequent INFECTION with the same PATHOGEN. Immunization may occur as a natural consequence of infection or through vaccination (also called inoculation). The IMMUNE SYSTEM creates unique antibodies, specialized proteins that attach to B-cell lymphocytes that circulate in the BLOOD and the LYMPH, in response to antigens present on the cell surfaces of the pathogen. The antibodies then respond to the presence of the ANTIGEN within the body, activating a rapid IMMUNE RESPONSE to contain and neutralize the pathogen before it establishes sufficiently to cause illness. A VACCINE contains a nonpathogenic preparation of an antigen to stimulate the same immune response without causing illness. Natural immunization is usually lifelong. Immunization acquired through vaccination may require a series of vaccinations or periodic booster vaccines to maintain adequate protection against infection.

See also ANTIBODY; ANTIBODY-MEDIATED IMMUNITY; B-CELL LYMPHOCYTE; CHILDHOOD DISEASES; LYMPHOCYTE; PREVENTIVE HEALTH CARE AND IMMUNIZATION.

incubation period The length of time between the exposure to a PATHOGEN and the appearance of symptoms or illness. Incubation periods vary from a few hours (illnesses such as CHOLERA and SHIGELLOSIS) to months (illnesses such as HEPATITIS C, TUBERCULOSIS, and AMEBIASIS). Some diseases, such as AIDS (acquired immunodeficiency syndrome) and HUMAN PAPILLOMAVIRUS (HPV), may have incubation periods of years. During the incubation period the pathogen replicates until its presence reaches a level that can overcome the immune system's efforts to contain it. Viral infections in particular may be contagious during the incubation period.

See also BACTERIA; FUNGUS; HIV/AIDS; INFECTION; PARASITE; VIRUS.

infection The invasion of the body by a PATHOGEN (microorganism capable of causing disease), sometimes called an infectious agent, that enters cells and attempts to reproduce or replicate itself. The pathogen may be a bacterium, FUNGUS (yeast or mold), VIRUS, PARASITE, or prion. Not all infections cause symptoms or illness, and some infections may be present in the body for an extended time before they cause disease. The length of time between the entrance of a pathogen into the body and the appearance of symptoms is the illness's INCUBATION PERIOD.

The IMMUNE SYSTEM detects and in some way contains most pathogens. INFLAMMATION and FEVER, for example, are ways in which the immune response creates an unfavorable environment for many pathogens. Though the common perception that symptoms such as fever and MUSCLE aches are the effects of the infection, they are often instead the immune system's methods for eliminating the pathogen before its presence can cause illness.

Sometimes an infection is able to evade the immune system's efforts to eliminate it, such as HIV (human immunodeficiency virus), the infection that ultimately results in AIDS (acquired immunodeficiency syndrome). HIV actually infects the cells of the immune system that would fight its presence, restructuring their functions so they are no longer effective.

See also ANTIBODY-MEDIATED IMMUNITY; BACTERIA; CELL-MEDIATED IMMUNITY; IMMUNIZATION.

influenza A common and potentially serious viral INFECTION, commonly called the flu, that

causes upper respiratory symptoms. Influenza viruses rapidly adapt and mutate, which gives them the perpetual ability to cause illness. There are three types of human influenza VIRUS—influenza A, influenza B, and influenza C. Influenza A viruses are primarily responsible for annual outbreaks of the flu, though influenza B viruses also cause illness.

Some strains of influenza A infect humans and some strains infect animals such as pigs (swine influenza virus) and poultry (avian influenza virus). Strains of influenza A that infect animals can sometimes mutate in ways that permit them to cross over to infect people, as happened in 1918 with the world's most severe influenza pandemic, known as the Spanish flu (because the first cases occurred in Spain), which researchers today believe mutated from a variety of swine influenza virus.

Symptoms and Diagnostic Path

Influenza is an illness of the upper respiratory tract, the symptoms of which tend to emerge rapidly and full-force. Symptoms of influenza include

- high FEVER (102°F or higher)
- severe HEADACHE
- muscle aches and JOINT PAIN
- nonproductive COUGH
- sore THROAT
- nasal and sinus congestion

Some people, especially young children, may experience NAUSEA and VOMITING. However, gastrointestinal symptoms are not characteristic of influenza, and their prominent presence suggests a different infection. There are several tests available for influenza, including rapid tests that the doctor can use in the office as well as blood tests.

Treatment Options and Outlook

Most often, the flu simply runs its course and treatment targets relieving symptoms such as fever and aches. Rest, fluids, and nutritious foods are important for helping the body to fight the virus. Secondary bacterial infections and other complications can occur and require appropriate treatment. ANTIBIOTIC MEDICATIONS are not effective for treating viruses, though the doctor may prescribe an antibiotic to treat a secondary bacterial infection that develops, such as PNEUMONIA or STREP THROAT. The most common complication of influenza is PNEUMOCOCCAL PNEUMONIA, a bacterial infection for which there is a one-time vaccine (though people who have lung disorders or respiratory compromise may need a second vaccine 10 years after the first vaccine).

The flu vaccine IMMUNIZATION remains the frontline of treatment for influenza. Each year researchers determine the two strains of influenza A and one strain of influenza B most likely to cause infection (based on complex algorithms of historic and projected viral cycles). Manufacturers then cultivate the three strains to create the year's VACCINE. This is a somewhat speculative approach, however, and the actual strains of influenza that surface may be entirely different. When the strains are similar to those in the vaccine the vaccine is highly effective in preventing or moderating influenza infection. When the strains are not at all close, the vaccine offers no protection from influenza infection. Because the influenza virus so rapidly mutates, each vaccine is effective only for a single flu season.

Antiviral medications ANTIVIRAL MEDICATIONS may shorten the course of illness and lessen the severity of symptoms when taken within 48 hours of the first symptoms and may prevent infection with influenza after exposure to someone who has the viral infection. Antiviral medications work by interfering with the mechanisms viruses use to alter the functions of their host cells, typically by blocking the action of key enzymes or proteins that the virus uses to instruct RNA to take over the host cell. Some antiviral medications are effective against influenza A (amantadine and rimantadine) and others against influenza B (zanamivir and oseltamivir). Further testament to the influenza virus's ability to mutate is the emergence of influenza virus strains that are resistant to amantadine and rimantadine.

Risk Factors and Preventive Measures

People at highest risk for influenza are the very young, the very old, and those who have compro-

mised immune function, such as people who have HIV/AIDS or CANCER or who take IMMUNOSUPPRESSIVE THERAPY after ORGAN TRANSPLANTATION. People who have DIABETES and other chronic health conditions also have increased risk for infection. Preventive measures to reduce the risk for influenza infection include

- frequent HAND WASHING with warm water and soap
- disinfecting common use surfaces such as doorknobs
- minimizing exposure to enclosed crowds of people during peak flu season (November through March in the United States)

Annual flu vaccines are currently the most effective method for preventing influenza.

See also BACTERIA; INFLUENZA PREVENTION; SNEEZE/COUGH ETIQUETTE.

L–M

listeriosis An illness that results from INFECTION with the bacterium *Listeria monocytogenes*. Listeriosis most often occurs as a foodborne illness and has the potential to cause serious symptoms. *L. monocytogenes* are normally present in soil and can contaminate milking equipment. Animals also can carry *L. monocytogenes* without illness. The most common sources of listeriosis are unpasteurized milk and cheeses and processed foods that become contaminated after processing, such as lunch meats served in delis and restaurants. Thorough cooking and pasteurization kill *L. monocytogenes* BACTERIA.

Symptoms and Diagnostic Path

Symptoms of listeriosis are often fairly severe and many people who develop the illness require hospitalization for treatment. Symptoms may include

- FEVER
- difficulty BREATHING (DYSPNEA)
- NAUSEA and VOMITING
- MUSCLE aches and JOINT PAIN

Symptoms may also be specific to the type of infection, such as MENINGITIS or PNEUMONIA. The diagnostic path includes BLOOD cultures and, when neurologic symptoms are present, LUMBAR PUNCTURE to examine and culture the spinal fluid. The presence of *L. monocytogenes* confirms the diagnosis.

Treatment Options and Outlook

Treatment is antibiotic therapy, intravenous when symptoms are serious and oral when symptoms are moderate. Ampicillin, erythromycin, and sulfamethoxazole/trimethoprim (SMZ-TMP) are the antibiotics most effective; the usual course of antibiotic therapy may be four to six weeks. Most people fully recover with appropriate ANTIBIOTIC MEDICATIONS.

Risk Factors and Preventive Measures

People most at risk for listeriosis are those who are IMMUNOCOMPROMISED, particularly people who have HIV/AIDS. Pregnant women are also more vulnerable to infection and can pass the infection to their unborn babies; researchers believe this is due to the changes that take place in a woman's body under the influence of the hormones of PREGNANCY. Some pregnant women can harbor *L. monocytogenes* bacteria without becoming ill, though pass the infection to their babies. Listeriosis can cause STILLBIRTH (fetal death) and serious neurologic problems in newborns after birth. Health experts caution pregnant women (and other people at increased risk for listeriosis) to eat lunch meats and hot dogs only that are thoroughly reheated, to eat only pasteurized cheeses, to drink only pasteurized milk, and to wash all vegetables and fruits before eating them including lettuce) as methods for reducing their exposure to *L. monocytogenes* infection.

See also FOODBORNE ILLNESSES; FOOD SAFETY; HORMONE; WATERBORNE ILLNESSES.

Lyme disease An illness that results from INFECTION with the bacterium *Borrelia burgdorferi* in North America and other *Borrelia* species in Europe. The bite of the *Ixodes scapularis* tick, common in wooded areas throughout the northern United States, spreads the infection. *B. burgdorferi* infection primarily causes flulike symptoms though may also affect the CENTRAL NERVOUS SYSTEM, cardiovascular system, and the joints.

Symptoms of Lyme disease begin 5 to 30 days after a tick bite, typically with a characteristic RASH

called erythema migrans. The rash starts at the site of the bite and looks somewhat like a bull's eye around the bite. The rash expands over five to seven days, becoming large and raised, and may burn or hurt. The rash may also spread to other parts of the body.

Other symptoms may include

- FEVER
- HEADACHE
- MUSCLE aches and JOINT PAIN
- LYMPHADENOPATHY (swollen LYMPH nodes)

Though these symptoms, including the rash, will go away without treatment, the infection remains in the body and extends its involvement. Untreated Lyme disease may cause

- NEUROPATHY (tingling and numbness in PERIPHERAL NERVES), ENCEPHALOPATHY (disturbances of BRAIN function), and MENINGITIS (INFLAMMATION of the membranes that surround the brain and SPINAL CORD)
- BELL'S PALSY (PARALYSIS of the facial muscles)
- arthritis (inflammation of the joints), particularly in the knees and hips
- PALPITATIONS, dizziness, and changes in BLOOD PRESSURE resulting from cardiovascular involvement

BLOOD tests confirm the diagnosis. Treatment with ANTIBIOTIC MEDICATIONS eliminates the infection. People who receive early diagnosis and treatment nearly always recover quickly and fully. When the infection has spread to multiple body systems, residual effects may continue for several months.

ANTIBIOTIC MEDICATIONS TO TREAT LYME DISEASE

amoxicillin	ampicillin
azithromycin	cefuroxime
doxycycline	

Tick precautions when hiking or camping in tick-infested areas are the most effective means of preventing Lyme disease. Such precautions include wearing long pants tucked into high boots or socks to prevent ticks from attaching to the lower legs, examining the entire body for ticks after activities of possible exposure, and immediately removing any attached ticks. Because early treatment can avert serious complications, anyone bitten by a tick who develops rash or flulike symptoms should receive a medical evaluation for the possibility of Lyme disease or for ANTIBIOTIC PROPHYLAXIS (preventive antibiotic therapy).

See also ROCKY MOUNTAIN SPOTTED FEVER.

malaria An illness that results from INFECTION with one of four *Plasmodium* parasites: *Plasmodium malariae, P. ovale, P. vivax,* and *P. falciparum*. Bites from the female *Anopheles* mosquito spread the infection from one person to another. Though malaria has not occurred naturally in the United States since the 1950s, travel to or immigration from regions of the world where malaria is endemic results in about 1300 cases of malaria in the United States each year.

Malaria can be serious or fatal without treatment and is a major cause of death worldwide, particularly in developing nations with limited access to medical resources. Malaria is particularly devastating in the Sahara and sub-Sahara regions of the African continent, where it claims the life of one child every 30 seconds. Extreme poverty, lack of medical resources, and environmental conditions in which mosquito populations flourish converge in these regions, maintaining an endemic presence of malaria that is the most extensive in the world.

Plasmodium parasites initially infect LIVER cells, where they reproduce. They then migrate into erythrocytes (red BLOOD cells), entering the blood circulation. The INCUBATION PERIOD ranges from 8 days to several months, after which flulike symptoms emerge that include

- FEVER and chills
- HEADACHE
- MUSCLE aches
- NAUSEA, VOMITING, and DIARRHEA
- JAUNDICE (yellow discoloration of the SKIN)
- tiredness or fatigue

Microscopic examination of a blood sample shows the parasites, confirming the diagnosis.

Early treatment with medications to kill the *Plasmodium* parasites is essential, particularly when the infective PARASITE is *P. falciparum,* which causes life-threatening illness. Because antimalarial medications are effective against the parasites in the blood, it is essential to continue treatment through several life cycles of the parasites to kill those emerging from the liver. Only one antimalarial medication, primaquine, can kill liver-based *Plasmodium*. The specific medications and length of treatment depend on the type of infection, region of the world where the person acquired the infection, and the person's age and other health circumstances.

MEDICATIONS TO TREAT MALARIA

atovaquone-proguanil	chloroquine
doxycycline	mefloquine
primaquine	quinine
sulfadoxine-pyrimethamine	

Aggressive mosquito-control measures are the most successful preventive approach. These measures include public health efforts to eradicate mosquito populations, such as through insecticide application and eliminating standing water that serves as mosquito breeding grounds, and personal prevention efforts, such as wearing clothing that protects against mosquito bites. People planning travel to regions where *Plasmodium* infection is possible should take prophylactic medications.

See also ERYTHROCYTE; TOXOPLASMOSIS; TYPHOID FEVER.

measles An illness resulting from INFECTION with the measles VIRUS. Once among the most common childhood diseases worldwide, measles (also called rubeola) now primarily exists in developing nations where it remains a leading cause of childhood blindness and death. Routine measles IMMUNIZATION, the standard of care since becoming available in the early 1960s, has eradicated measles from much of the industrialized world. In the United States children generally receive measles VACCINE through the combination MMR (measles-mumps-rubella) vaccine.

Measles is one of the most highly contagious infections and spreads through droplet contamination via airborne transmission (sneezing and coughing) as well as direct contact. The virus invades the lining of the THROAT and the LUNGS, where it replicates. The virus then uses the lymphatic system to enter the BLOOD circulation, after which prodrome symptoms emerge that include

- FEVER
- sensitivity to light (PHOTOPHOBIA)
- congestion of the nasal passages and profuse nasal discharge
- nonproductive COUGH

Within two days the characteristic measles RASH emerges. This red, itchy rash starts at the hairline on the scalp and spreads to cover the entire body, including the palms of the hands and soles of the feet. The course of illness runs about 10 days after the rash begins. The infection is most contagious during the prodrome stage, though contagiousness continues through the rash stage. Diagnosis is clinical based on the characteristic nature of symptoms and history of exposure.

The risk for complications from measles is high, primarily because the measles virus's use of the IMMUNE SYSTEM to distribute itself compromises the IMMUNE RESPONSE, lowering resistance to infection from other pathogens. As a consequence secondary bacterial infections, notably OTITIS media (middle EAR infection) and PNEUMONIA, are common. Such bacterial infections require treatment with ANTIBIOTIC MEDICATIONS, though antibiotics do not treat measles. The measles virus may also cause viral pneumonia and MENINGITIS. IMMUNOGLOBULIN may prevent or moderate illness in people exposed to measles. However, ANTIVIRAL MEDICATIONS are not effective. Complications are more common in people who have vitamin A deficiency, though doctors do not know whether vitamin A supplementation during illness with measles decreases this risk.

See also BACTERIA; CHICKENPOX; MUMPS; PATHOGEN; PREVENTIVE HEALTH CARE AND IMMUNIZATION; SNEEZE/COUGH ETIQUETTE; VITAMINS AND HEALTH.

meningitis INFLAMMATION of the MENINGES, the membranes that surround the BRAIN and SPINAL CORD. Meningitis may result from bacterial, viral, or fungal INFECTION. Viruses are the most common causes of meningitis and can be highly contagious.

Enteroviruses and *Haemophilus influenzae* type B (Hib) VIRUS are the common viral causes, though many viruses can cause meningitis. Bacterial meningitis may be life threatening and requires immediate treatment with intravenous ANTIBIOTIC MEDICATIONS. The contagiousness of bacterial meningitis depends on the BACTERIA.

Symptoms and Diagnostic Path

Symptoms of meningitis tend to be milder with viral meningitis. They may appear gradually and include

- FEVER
- severe HEADACHE
- NAUSEA and VOMITING
- sore or stiff neck, or inability to touch the chin to the shoulder or chest
- agitation and confusion
- inability to remain alert or awake

LUMBAR PUNCTURE, which may reveal elevated cerebrospinal pressure and evidence of infection such as white BLOOD cells or the presence of bacteria, is the definitive diagnostic procedure.

Treatment Options and Outlook

Bacterial meningitis requires immediate treatment with antibiotic medications. Viral meningitis is self-limiting and usually improves on its own as the illness runs its course. Supportive treatment for viral meningitis may include intravenous fluids to maintain adequate HYDRATION. Complications that may occur with meningitis regardless of the causative PATHOGEN include swelling of the brain tissue, seizures, and diminished CONSCIOUSNESS. With appropriate treatment many people recover fully; some people have residual complications such as cognitive dysfunction, VISION IMPAIRMENT, or HEARING LOSS.

Risk Factors and Preventive Measures

The primary risk for meningitis is infection with any virus that can involve the meninges. Meningitis sometimes occurs in clusters of cases in settings where people live in close contact, such as college dormitories. People who are IMMUNOCOMPROMISED have increased risk for meningitis and many other kinds of infections. The most effective prevention measures are those that reduce the risk for acquiring viral infections—frequent HAND WASHING and diligent PERSONAL HYGIENE—and early treatment for symptoms of bacterial meningitis.

See also COGNITIVE FUNCTION AND DYSFUNCTION; ENCEPHALITIS; FUNGUS; VIRUS.

microbe A living organism, also called a microorganism, that is too small to see with the unaided EYE. Most microbes are single-cell or simple multiple cell organisms. Common microbes include BACTERIA, fungi (yeasts and molds), viruses, PROTOZOA, and algae. Microbes are abundant in the natural environment as well as the environment of the human body. Many microbes can cause INFECTION and illness in humans. Dutch scientist Antonie van Leeuwenhoek (1632–1723) identified many microbes using microscopes he constructed himself, paving the way for what would become the foundation of understanding for many disease processes.

See also FUNGUS; VIRUS.

mononucleosis, infectious An illness that results from INFECTION with the EPSTEIN-BARR VIRUS. Infectious mononucleosis is most prevalent among adolescents and young adults though may occur at any age. The infection spreads through contact with saliva; among young people and within families, sharing drinks and food are common means of contracting the illness. The Epstein-Barr VIRUS infects B-cell lymphocytes, also called mononuclear (single nucleus) lymphocytes, which is what gives the illness its name.

Symptoms and Diagnostic Path

The symptoms of infectious mononucleosis are flulike and generally mild to moderate in severity. Many people do not realize they have the illness. Symptoms include

- low-grade FEVER
- HEADACHE
- sore THROAT (PHARYNGITIS)
- fatigue
- cervical and axillary LYMPHADENOPATHY (swollen LYMPH nodes in the neck and underarms)

- abdominal tenderness
- slight JAUNDICE (yellow discoloration of the SKIN)

The diagnostic path includes BLOOD tests; the presence of abnormal lymphocytes and antibodies for Epstein-Barr virus confirms the diagnosis. Some people have mild HEPATITIS (INFLAMMATION of the LIVER), which blood tests also confirm, and mild to moderate SPLENOMEGALY (enlarged SPLEEN), which the doctor can detect with palpation (by feeling the abdomen).

Treatment Options and Outlook

Treatment is supportive, with rest and plenty of fluids. The course of illness may run three to six weeks, during which time the person is contagious and can spread the infection to other people. Most people recover fully, though it may take several months to feel back to normal. Though infectious mononucleosis is generally a benign, self-limiting viral infection, the Epstein-Barr virus remains in the body for life and is linked to certain kinds of cancer (notably Burkitt's lymphoma). A person can have infectious mononucleosis only once; the body develops IMMUNITY with infection.

Risk Factors and Preventive Measures

The Epstein-Barr virus is ubiquitous in the world; avoiding infection is nearly impossible. Measures such as frequent HAND WASHING and appropriate SNEEZE/COUGH ETIQUETTE reduce the risk for passing the infection to others. Adequate rest during the active illness reduces the risk for complications.

See also ANTIBODY; ANTIBODY-MEDIATED IMMUNITY; B-CELL LYMPHOCYTE; LYMPHOCYTE.

mumps An illness resulting from the mumps VIRUS, which primarily infects the SALIVARY GLANDS and may also involve the PANCREAS, TESTICLES (men), OVARIES (women), and sometimes the KIDNEYS. The mumps virus may also invade the CENTRAL NERVOUS SYSTEM, causing NEURITIS and ENCEPHALITIS. Since the advent of the mumps VACCINE in the early 1980s, mumps infections have become uncommon in the United States and now tend to occur in adults who did not have the INFECTION as children. Infection with mumps confers lifelong IMMUNITY, as does vaccination.

The mumps virus is contagious through contact with saliva, either direct or via airborne droplets. After an INCUBATION PERIOD of 14 to 21 days, symptoms emerge that include

- painful swelling of the parotid salivary glands at the base of the EAR
- HEADACHE
- sore THROAT
- FEVER

Swollen testicles are common in boys and lower abdominal PAIN, reflecting ovarian swelling, is common in girls. The classic "eat a pickle" test for mumps has some merit in that eating sour foods greatly intensifies the pain. However, the doctor usually makes the diagnosis on the basis of the symptoms and history of exposure or lack of IMMUNIZATION. Treatment targets symptom relief. Most people recover fully. A small percentage of people, usually adults, who acquire mumps infection develop neurosensory HEARING LOSS that is usually temporary. Mumps infection in both testicles (bilateral testicular mumps) can cause sterility, though this is uncommon. Though mumps encephalitis and MENINGITIS are serious complications, they are seldom fatal and most people recover without long-term consequences.

See also CHICKENPOX; CHILDHOOD DISEASES; MEASLES.

N–O

necrotizing fasciitis A rare but serious bacterial INFECTION of the fascia, the layer of connective tissue that covers, separates, and connects the muscles and other musculoskeletal structures. In necrotizing fasciitis a combination of aerobic and anaerobic bacterial activity produces an abundance of nitrogen, hydrogen, and methane gases. These gases act to suppress the activity of white BLOOD cells that ordinarily would move in to fight the infection. Necrotizing fasciitis is most commonly an OPPORTUNISTIC INFECTION that develops in people who have DIABETES, HIV/AIDS, and other circumstances of immunocompromise.

Nearly always the infection arises at or near the site of a wound, either accidental (more common) or surgical. Symptoms include sudden, severe PAIN at the site along with redness and slight swelling. The person generally feels and looks well in the early stages of the infection, then suddenly becomes critically ill. The redness of the RASH becomes purple, and the SKIN is odd to the touch. Often there is loss of sensation (traumatic ANESTHESIA) in the area. Necrotizing fasciitis moves very rapidly along the fascia into the deep tissues; the farther into the body it goes, the faster its progression because the anaerobic conditions (lack of oxygen) support its growth. Diagnosis is difficult in the early stages but unmistakable in the later stages. Blood cultures and cultures of tissue samples from the innermost edges of the infection generally reveal the causative BACTERIA, which allows doctors to choose effective ANTIBIOTIC MEDICATIONS.

Treatment is multifocused and includes intravenous antibiotics, usually multiple drugs, to attack the various types of bacteria involved in the infection as well as surgery to expose the infection to air (which reduces the ability of anaerobic bacteria to flourish) and remove dead and infected tissue so only healthy tissue remains. The surgical wounds are often significantly larger than the surface appearance of the infection would suggest because so much of the infection is deep within the body. Multiple operations are often necessary. Treatment with hyperbaric oxygen speeds improvement in some people.

With early detection and aggressive treatment that keeps necrotizing fasciitis fairly localized, the likelihood for recovery is good. When infection is extensive and other health conditions exist that challenge the IMMUNE RESPONSE, about 20 percent of people survive necrotizing fasciitis. Because researchers do not understand the complexity of circumstances that allows necrotizing fasciitis to develop, there are no methods for preventing infection. People who have any degree of immunocompromise should carefully monitor any wounds and seek prompt medical care for those that do not seem to follow a normal path of HEALING.

See also ANTIBIOTIC RESISTANCE; BOTULISM; GANGRENE; IMMUNOCOMPROMISED.

normal flora The BACTERIA, fungi, and other microorganisms naturally present within the environment of the healthy body. Normal flora exist on the surface of the SKIN, within natural cavities such as the NOSE and MOUTH, in the gastrointestinal tract, and in the reproductive tract. These beneficial microbes participate in the body's IMMUNE RESPONSE, digestive functions, and reproductive functions, among others.

Normal flora microbes exist in a balance that prevents one type of MICROBE from overpowering another. Circumstances that change this balance may allow illness to develop. Antibiotic therapy targets bacteria, for example, though antibiotics

cannot distinguish between normal flora and pathogenic bacteria. So ANTIBIOTIC MEDICATIONS, particularly broad-spectrum antibiotics, kill bacteria in the gastrointestinal tract and the reproductive tract at the same time they kill pathogenic bacteria. The result may be DIARRHEA or yeast VAGINITIS.

See also FUNGUS; INFECTION.

nosocomial infections Illnesses that result from INFECTION acquired in a hospital, skilled nursing facility, or other health-care facility. The PATHOGEN is typically bacterial, viral, or fungal. Many pathogens that cause nosocomial infections are resistant to common methods of treatment. The most common causes of nosocomial infections are

- invasive procedures ranging from intravenous (IV) lines and urinary catheters to surgery
- environmental factors such as air-conditioning and heating systems that harbor and distribute pathogens
- poor hygiene practices by staff (inadequate HAND WASHING, improper disposal of contaminated items)
- inappropriate separation of patients (such as medical patients roomed with surgical patients)

The risk for acquiring a nosocomial infection correlates directly to the length of time the person remains in the hospital or care facility—the longer the stay, the greater the risk. About 2 million people acquire nosocomial infections in the United States each year. Prevention efforts include improved infection control procedures and education for hospital and care facility staff.

See also ANTIBIOTIC RESISTANCE; BACTERIA; FUNGUS; LEGIONNAIRES' DISEASE; OPPORTUNISTIC INFECTION; VIRUS.

opportunistic infection Illness that develops in a person who is IMMUNOCOMPROMISED as a result of exposure to an otherwise benign MICROBE or a PATHOGEN a healthy IMMUNE SYSTEM could contain or eradicate. Opportunistic infections commonly occur in people who have HIV/AIDS, are receiving IMMUNOSUPPRESSIVE THERAPY after ORGAN TRANSPLANTATION, or are undergoing certain kinds of treatment for cancer. The weakened state of the IMMUNE SYSTEM allows infections to take hold as well as makes fighting the INFECTION more difficult.

COMMON OPPORTUNISTIC INFECTIONS

CANDIDIASIS	CYTOMEGALOVIRUS (CMV) INFECTION
HERPES SIMPLEX infection	COCCIDIOIDOMYCOSIS
CRYPTOCOCCOSIS	*Pneumocystis carinii* PNEUMONIA
TOXOPLASMOSIS	TUBERCULOSIS

See also NOSOCOMIAL INFECTION.

P–R

parasite An organism that requires coexistence with another organism for its survival. The parasite typically draws nourishment and other needs from its host organism without contributing in return to the host's survival. Some parasites can survive away from their hosts for limited periods of time or defined portions of their life cycles. Some parasites are host-specific whereas others can adapt to various hosts.

Pathogenic parasites are those that cause INFECTION and disease. Common pathogenic parasites include flukes, worms, and PROTOZOA (amebas). They may infect the SKIN or migrate to internal organs such as the LUNGS, LIVER, or BRAIN, where they often form cysts. Treatment for parasitic infections and illnesses depends on the parasite and the illness.

People who travel to tropical regions or areas where community sanitation is substandard may acquire parasitic infections otherwise uncommon in their home regions. Many systemic parasitic infections cause gastrointestinal symptoms such as DIARRHEA. These infections are usually contagious, spread through fecal–oral contact (contact with surfaces and substances such as food or water that are contaminated with particles of feces). Diligent PERSONAL HYGIENE, especially HAND WASHING, and appropriate FOOD SAFETY practices are key preventive measures.

COMMON PARASITIC INFECTIONS

AMEBIASIS	BABESIOSIS
CRYPTOSPORIDIOSIS	CYCLOSPORIASIS
GIARDIASIS	MALARIA
microsporidiosis	PEDICULOSIS
SCABIES	TRICHOMONIASIS

See also BACTERIA; FUNGI; MICROBE; VIRUS.

pathogen A MICROBE capable of causing illness. The most common pathogens are BACTERIA, fungi, parasites, and viruses. The process through which a pathogen, also called an infectious agent, causes illness is pathogenesis. The body attempts to protect itself from pathogens through numerous mechanisms, key among them being ANTIBODY-MEDIATED IMMUNITY and CELL-MEDIATED IMMUNITY. Vaccines and treatments with ANTIBIOTIC MEDICATIONS, ANTIVIRAL MEDICATIONS, and ANTIFUNGAL MEDICATIONS are among the methods available to contain and eradicate pathogens once they establish infection in the body.

See also FUNGUS; PARASITE; PROTOZOA; VACCINE; VIRUS.

pertussis An illness resulting from INFECTION with the VIRUS *Bordetella pertussis*. Pertussis is among the childhood diseases for which routine IMMUNIZATION is the standard of care in the United States. The hallmark of the illness is a rapid, violent cough that causes the person to make a "whooping" sound when trying to breathe through the coughing, hence the common term whooping cough. The cough can be severe enough to prevent BREATHING. Pertussis was once a leading cause of death among children under age 5. Though immunization has dramatically reduced infection, pertussis may still be fatal in very young children and very old adults. IMMUNITY, either natural (following infection and illness) or via VACCINE, lasts about 12 years.

The unmistakable cough is the primary symptom and begins about seven days after exposure. In untreated pertussis, the cough worsens rapidly and may continue for as long as eight weeks. Many people also experience VOMITING with the coughing. The doctor often makes the diagnosis on the basis

of the cough, though cultures taken from the MOUTH and NOSE may provide confirmation. Cultures are positive in about 80 percent of people.

Treatment in the early stages of pertussis is ANTIBIOTIC MEDICATIONS, typically erythromycin or trimethoprim and sulfamethoxazole (TMP-SMZ). The further into the course of illness, the less effective antibiotics become, however. The infection causes the nasal passages, THROAT, bronchi, and bronchioles to ooze fluid that clogs the airways; the cough is the body's attempt to remove the fluid to permit free breathing. A profusely runny nose (rhinorrhea) is the earliest symptom of pertussis though often is perceived as a cold until the cough begins. Antibiotic therapy can substantially shorten the course and lessen the severity of illness. Most people recover fully with appropriate treatment, particularly when treatment begins early.

See also CHILDHOOD DISEASES; DIPHTHERIA; PREVENTIVE HEALTH CARE AND IMMUNIZATION.

pneumococcal pneumonia An illness resulting from INFECTION with the bacterium *Streptococcus pneumoniae*, which is normally present in the mucous membranes of the NOSE and sinuses. Researchers do not know what processes occur in the body that allow *S. pneumoniae* to shift from NORMAL FLORA to causing infection in its native environment. Pneumococcal pneumonia is a serious upper respiratory illness that can invade the LUNGS and spread to the BRAIN (causing MENINGITIS) and middle EAR (causing OTITIS media). Pneumococcal pneumonia can also cause SEPTICEMIA, a life-threatening illness of widespread bacterial infection that involves multiple organ systems.

Symptoms and Diagnostic Path

Symptoms begin suddenly and are usually severe. They include

- a shaking chill followed immediately by sudden high FEVER
- nonproductive COUGH
- difficulty BREATHING (DYSPNEA) and CHEST PAIN
- HEADACHE
- NAUSEA and VOMITING
- fatigue

The diagnostic path includes chest X-RAY and BLOOD or fluid tests to determine the presence of *S. pneumoniae*. Because symptoms are severe and the risk for complications is high, doctors typically begin immediate treatment with ANTIBIOTIC MEDICATIONS. Symptoms that dramatically improve with the first 24 hours of treatment further confirm the diagnosis.

Treatment Options and Outlook

Penicillin is the antibiotic of first choice for treatment, though about 25 percent of *S. pneumococcal* strains are now resistant to it. Most resistant strains are sensitive to other antibiotic medications. The antibiotic of last resort is vancomycin, which doctors reserve for pneumonia that does not respond to treatment with any other antibiotics. With appropriate antibiotic therapy many people fully recover from pneumococcal pneumonia, though it is important to take the full course of antibiotics even after symptoms are gone. Pneumococcal pneumonia can be fatal.

ANTIBIOTIC MEDICATIONS TO TREAT PNEUMOCOCCAL PNEUMONIA

cefotaxime	ceftizoxime
ceftriaxone	clindamycin
erythromycin	gatifloxacin
grepafloxacin	levofloxacin
penicillin	moxifloxacin
sparfloxacin	vancomycin

Risk Factors and Preventive Measures

People most vulnerable to pneumococcal pneumonia are the very young, the very old, and those who are IMMUNOCOMPROMISED. The pneumococcal VACCINE, administered each year, can prevent *S. pneumoniae* infection.

See also ANTIBIOTIC RESISTANCE; INFLUENZA; INFLUENZA PREVENTION.

prion A protein fragment that becomes a PATHOGEN. Prion illnesses affect the BRAIN and cause extensive damage to brain tissue, causing it to become spongy in appearance. Though prion illnesses are not contagious in typical fashion, introduction of infectious prions into healthy brain tissue transmits the INFECTION. Because of these characteristics, researchers call prion illnesses

transmittable spongiform encephalopathies (TSEs). Some prion diseases are inherited and others are acquired. The most notorious prion illness is variant Creutzfeldt-Jakob disease (vCJD), acquired through the consumption of beef from cattle that have bovine spongiform encephalopathy (BSE), commonly called mad cow disease. Prions are highly resistant to disinfectants and sterilization procedures. Many hospitals now use disposable instruments for brain surgery to reduce the risk for transmitting a prion disease through an OPERATION.

See also CREUTZFELDT-JAKOB DISEASE (CJD); FOOD SAFETY.

prodrome The stage of illness immediately before the emergence of full symptoms. Prodrome is particularly prominent in herpesvirus INFECTION, which features tingling and irritation at the sites where herpes blisters are about to erupt. Prodrome occurs with many viral infections, such as MEASLES and CHICKENPOX. Often these infections are most contagious during the prodrome.

See also BLISTER; HERPES SIMPLEX; HERPES ZOSTER; GENITAL HERPES.

protozoa Single-celled organisms such as amebas. Many protozoa are parasitic and require host organisms for survival. Some protozoa are pathogenic, notably those that cause MALARIA and infections such as AMEBIASIS, BABESIOSIS, and GIARDIASIS. Some protozoal infections are self-limiting and others require treatment with medications such as antibiotics.

See also ANTIBIOTIC MEDICATIONS; BACTERIA; FUNGUS; PARASITE; VIRUS.

rabies A potentially fatal illness resulting from INFECTION with the rabies VIRUS, which belongs to the *Lyssavirus* viral family. Rabies is very rare in people though a common infection in wild animals who can transmit the infection to unvaccinated pets such as dogs and cats or to people through bites. Raccoons, skunks, coyotes, and bats are reservoirs for the rabies virus; though infected with the rabies virus, these animals do not themselves become ill with rabies. Nearly any animal may acquire rabies infection as a result of contact with saliva or other secretions from an infected animal, usually a bite.

In animals and humans the rabies virus infects the CENTRAL NERVOUS SYSTEM. It travels via the PERIPHERAL NERVES to the BRAIN, where it replicates within brain neurons (NERVE cells). Symptoms of illness generally appear one to three months after exposure, though the INCUBATION PERIOD may be as short as a few days or as long as several years. Once symptoms appear rabies is fatal. The illness of rabies is ENCEPHALITIS.

The most effective treatment for rabies infection in people is postexposure prophylaxis, which consists of one injection of human rabies IMMUNOGLOBULIN and five injections of rabies VACCINE administered at regular intervals after a bite from a potentially infected animal. The vaccine injections are given in the upper arm and are similar in discomfort to receiving a tetanus shot. The course of postexposure prophylaxis covers 28 days and appears to be 100 percent effective. People at high risk for rabies exposure, such as those who work with animals, can receive rabies vaccinations to prevent infection, though they also need postexposure prophylaxis if bitten.

See also IMMUNIZATION.

retroviruses See VIRUS.

Rocky Mountain spotted fever An illness resulting from INFECTION with the bacterium *Rickettsia rickettsii*. Tick bites spread Rocky Mountain spotted FEVER, so-named because of the characteristic RASH the illness causes. Symptoms generally appear within five days of a tick bite and include

- fever
- slight RASH
- NAUSEA and VOMITING
- severe HEADACHE
- MUSCLE PAIN

Symptoms become rapidly more severe as the illness progresses. Diagnosis is primarily clinical, based on the presentation of symptoms in combination with a history of tick bite or exposure to settings where tick bites are possible (such as hiking or camping in wooded areas). Treatment is prompt administration of doxycycline or tetracycline, ANTIBIOTIC MEDICATIONS that are especially

effective against *R. rickettsii*. Rapid improvement of symptoms confirms the diagnosis before BLOOD tests are able to do the same.

Most people fully recover with appropriate antibiotic treatment. However, Rocky Mountain spotted fever is life threatening for people who have G6PD DEFICIENCY, an inherited condition in which there is a lack of an enzyme important for maintaining red blood cells (erythrocytes). Age extremes (very young or very old) and chronic ALCOHOLISM are other factors that increase the severity of illness. Delayed treatment of Rocky Mountain spotted fever often results in multiple organ failure, requiring intensive medical treatment and a long recovery.

See also BACTERIA; ERYTHROCYTE; GENETIC DISORDERS; HUMAN EHRLICHIOSIS.

rubella An illness resulting from INFECTION with the rubella virus, a member of the *Rubivirus* viral family. Rubella, also called three-day MEASLES or German measles (because German researchers were the first to identify rubella as an illness separate from measles), is a mild course of illness in most people. However, the infection can cause serious BIRTH DEFECTS, collectively called congenital rubella syndrome, in a developing FETUS when a pregnant woman becomes infected during the first trimester of PREGNANCY.

Rubella is fairly contagious and spreads primarily through droplet inhalation (airborne transmission). The INCUBATION PERIOD is 14 to 21 days, after which most people experience low-grade FEVER; LYMPHADENOPATHY (swollen LYMPH nodes); and a red, slightly bumpy RASH that begins on the face and spreads to cover the entire body. Adults who get rubella often have PAIN and inflammation in the joints that continues for up to six weeks after other symptoms abate. Infection conveys lifelong IMMUNITY.

Rubella is among the diseases for which children in the United States receive routine IMMUNIZATION. This is particularly important because of the risk rubella infection presents to the unborn fetus. Congenital rubella syndrome affects about 90 percent of babies born to women who contract rubella during the first trimester of pregnancy. The syndrome's key features are

- HEARING LOSS, often profound (deafness)
- cataracts, GLAUCOMA, and RETINOPATHY
- pulmonary artery stenosis, ventral septal defect (VSD), patent ductus arteriosus (PDA), and other HEART anomalies
- impaired immune function
- early childhood development of type 1 DIABETES

Congenital rubella syndrome often causes lifelong health problems for affected children.

See also CATARACT; CATARACT EXTRACTION AND LENS REPLACEMENT; CHILDHOOD DISEASES; CONGENITAL HEART DISEASE; MEASLES; MUMPS; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS; SCARLET FEVER.

S

salmonellosis An illness resulting from INFECTION with any of the numerous strains of *Salmonella* BACTERIA. *Salmonella* are common in the feces of birds and animals. Salmonellosis is most often a foodborne illness acquired through eating raw eggs, unpasteurized dairy products, and undercooked poultry. Reptiles kept as pets, such as turtles and iguanas, also carry *Salmonella*. Once salmonellosis develops, the infected person can spread it to other people.

The INCUBATION PERIOD (time between exposure and illness) is often less than 12 hours. The most common symptom of salmonellosis is DIARRHEA, which may be bloody or profuse. Other symptoms include abdominal discomfort, NAUSEA, VOMITING, and FEVER. The course of illness is self-limiting and runs four to seven days in otherwise healthy people. In people who are IMMUNOCOMPROMISED salmonellosis may occur as an OPPORTUNISTIC INFECTION that causes significant illness. Because salmonellosis is self-limiting, doctors do not usually prescribe ANTIBIOTIC MEDICATIONS to treat it even though the cause is bacterial. Researchers have discovered that the *Salmonella* bacteria remain longer in the bodies of people who receive antibiotics for salmonellosis, extending the possibility of spreading the infection to other people.

The most effective approach is prevention through proper food handling and diligent PERSONAL HYGIENE. Thorough cooking kills *Salmonella*. FOOD SAFETY procedures include

- washing the hands with soap and warm water before and after handling food
- thoroughly rinsing fresh fruits and vegetables in running water before eating or preparing them for meals
- using separate food preparation surfaces, such as cutting boards, and utensils for poultry and meats
- thoroughly cooking eggs, poultry, and other animal-based foods

See also FOODBORNE ILLNESSES; WATERBORNE ILLNESSES.

scarlet fever An illness resulting from INFECTION with group A beta-hemolytic streptococcal BACTERIA that occurs as a complication of STREP THROAT. Scarlet FEVER begins with the same symptoms as strep THROAT—sudden onset of fever and often severe throat PAIN. Within two days a RASH erupts, starting on the chest and back and spreading to cover the entire body. The key characteristic of the rash is that it feels like sandpaper to the touch. Other symptoms of scarlet fever include

- bright red, inflamed ("strawberry") tongue
- bright red color to the natural creases in the SKIN (under the arms and in the groin)
- HEADACHE
- peeling of the skin on the fingertips, on the tips of the toes, and in the creases of the groin

Scarlet fever, like strep throat, is contagious and spreads among people through airborne transmission or direct contact with saliva (such as through shared food or eating utensils). The diagnostic path includes culture of the throat to detect the presence of group A strep bacteria, though the symptoms are so characteristic the doctor can usually make the diagnosis on the basis of their presence (clinical diagnosis).

Treatment is with ANTIBIOTIC MEDICATIONS, typically penicillins or erythromycin. Most people rapidly and fully recover with appropriate antibiotic therapy. Though the infection may resolve without treatment, the risk is very high for the strep bacteria to migrate to other locations in the body, notably the HEART valves where it causes RHEUMATIC HEART DISEASE. The infection may also spread to the joints, causing INFECTIOUS ARTHRITIS.

See also PHARYNGITIS; SNEEZE/COUGH ETIQUETTE; TONSILLITIS.

septicemia A life-threatening bacterial INFECTION that invades the BLOOD circulation, resulting in spreading the infection throughout the body. Septicemia, also called bacteremia, typically arises as a complication of localized bacterial infection. The onset and progression of septicemia are rapid and can result in septic SHOCK, ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS), and death within hours. Treatment requires hospitalization, usually in an intensive care unit, with administration of intravenous ANTIBIOTIC MEDICATIONS as well as other medications to sustain vital functions such as HEART RATE and BLOOD PRESSURE. People who recover from septicemia tend to have a long path of recuperation before they are able to return to regular activities.

See also DISSEMINATED INTRAVASCULAR COAGULOPATHY (DIC); NECROTIZING FASCIITIS; TOXIC EPIDERMAL NECROLYSIS; TOXIC MEGACOLON; TOXIC SHOCK SYNDROME.

severe acute respiratory syndrome (SARS) A life-threatening illness resulting from INFECTION with the VIRUS SARS-associated coronavirus (SARS-CoV). The first outbreak of SARS occurred in 2003 and sickened more than 8,000 people in Asia, Europe, and South America. The handful of people infected in the United States acquired SARS during travel to countries experiencing outbreaks.

Infection occurs through close contact; SARS-CoV spreads through airborne droplets as well as direct touch with saliva and other bodily secretions that shed the virus. Symptoms appear 2 to 10 days after infection and begin with HEADACHE, general MUSCLE aches and JOINT PAIN, sore THROAT, and moderate FEVER. Within a few days shortness of breath (DYSPNEA) develops and may result in HYPOXIA (insufficient oxygen entering the BLOOD circulation for distribution to organs and tissues. Blood tests confirm the presence of SARS-CoV.

Treatment is primarily supportive; ANTIVIRAL MEDICATIONS may lessen the severity of symptoms. Some people require hospitalization in an intensive care unit with MECHANICAL VENTILATION and other medical care to support respiration and other vital functions while the illness runs its course. PNEUMONIA is the most common complication. The course of illness may run several weeks. Most people recover, though may require several months of recuperation before feeling well enough to return to their normal activities.

See also INCUBATION PERIOD.

shigellosis An illness resulting from INFECTION with any of numerous strains of *Shigella* BACTERIA. Shigellosis most commonly occurs as a foodborne illness, producing symptoms of FEVER, abdominal cramping, and bloody DIARRHEA within about 12 hours of infection with the bacteria. The illness is generally self-limiting, running its course in five to seven days. Most people recover fully, though for a small percentage the bacteria infect other areas of the body such as the joints, causing the chronic condition REITER'S SYNDROME.

Doctors may prescribe ANTIBIOTIC MEDICATIONS for the very young, the very old, and people who are IMMUNOCOMPROMISED or who have unusually severe and extended symptoms. Ampicillin, trimethoprim/sulfamethoxazole (TMP-STZ) combination, and ciprofloxacin are among the antibiotics doctors more commonly prescribe. Diligent PERSONAL HYGIENE and frequent HAND WASHING are the most effective means to curtail the spread of shigellosis from one person to another.

See also ANTIBIOTIC RESISTANCE; FOODBORNE ILLNESSES; FOOD SAFETY; WATERBORNE ILLNESSES.

smallpox An illness resulting from INFECTION with the *Variola* VIRUS. Though smallpox was once a much-feared and leading cause of death worldwide, aggressive vaccination efforts resulted in the World Health Organization's determination of its eradication as a naturally occurring disease in

1980. The last smallpox infection to occur in the United States was in 1949; the last smallpox infection in the world was in 1977 (Somalia).

The name derives from the characteristic appearance of small sores that BLISTER and then crust, or pox, on the body when illness emerges. The sores, along with FEVER, are the primary symptom. They are also the means by which the virus sheds; contact with the sores or the fluids they contain spreads the virus and the infection. Throughout history until its eradication in the 20th century, smallpox claimed the lives of a third of those infected and often left disfiguring scars on those who survived.

Because the risk for complications is relatively high with the smallpox VACCINE and there are no smallpox infections worldwide, routine vaccination for smallpox no longer occurs. Smallpox reemerged as a potential public health concern in the early 2000s with worries that it, along with other infectious pathogens such as ANTHRAX, could be used as a biologic weapon or bioterrorism agent. Governments around the world have prepared emergency response plans to cope with such potential actions. Though when smallpox occurred naturally as a disease there were no known treatments, researchers believe modern ANTIVIRAL MEDICATIONS would be effective against smallpox infection today.

See also IMMUNIZATION; PATHOGEN.

sneeze/cough etiquette A method of PERSONAL HYGIENE to help prevent the spread of INFECTION. Sneezing and coughing are among the mechanisms the body uses to expel bacterial and viral particles in illnesses such as COLDS and INFLUENZA. However, these particles spread the infection to others who breathe them in with the air or touch surfaces on which they land. Health experts recommend these procedures to reduce the risk of spreading infection through sneezing and coughing:

- SNEEZE or COUGH into a tissue that covers the NOSE and MOUTH, then discard the tissue and wash the hands with soap and warm water.
- Sneeze or cough into the crook of the arm, which is less likely to be a point of contact with surfaces and other people.
- Avoid shaking hands with other people during illnesses that cause sneezing or coughing.

See also BACTERIA; VIRUS.

strep throat An INFECTION of the pharynx (throat), also called streptococcal PHARYNGITIS, with various strains of group A beta-hemolytic streptococcal BACTERIA. Strep throat is highly contagious through contact with saliva and requires treatment with ANTIBIOTIC MEDICATIONS to prevent potentially serious complications such as RHEUMATIC HEART DISEASE.

Symptoms and Diagnostic Path

The symptoms of strep throat come on suddenly, usually within five days of exposure to the infection. A characteristic indication of strep throat is the appearance of symptoms without other cold-like symptoms. Only about 5 percent of sore throats (pharyngitis) are strep throat; most sore throats are viral infections. Key symptoms of strep throat include

- FEVER
- moderate to severe throat PAIN
- difficulty swallowing
- HEADACHE
- ABDOMINAL PAIN and VOMITING
- enlarged, painful LYMPH nodes in the neck
- MUSCLE aches and JOINT pain

Symptoms generally peak 48 hours after they first appear. The throat looks very red and may have pockets of pus (white patches or streaks), particularly on the tonsils. However, the throat's appearance is not diagnostically conclusive. A rapid ANTIGEN test, which produces results in minutes from a swab of the throat, is fairly accurate when positive but inaccurate when negative. A culture of the throat provides definitive diagnosis.

Treatment Options and Outlook

Antibiotic medications are necessary to treat strep throat. Because antibiotics do not help viral infections of the throat and because antibiotic-resistant strains of strep are beginning to appear, doctors

tend to wait for the throat culture results before prescribing antibiotic medications unless the person has a history of strep throat.

ANTIBIOTIC MEDICATIONS TO TREAT STREP THROAT	
ampicillin	azithromycin
cefaclor	cefazolin
cefuroxime	cephalexin
clarithromycin	penicillin VK

Most people recover fully with appropriate antibiotic therapy, with symptoms dramatically improved within 48 hours of starting the antibiotic. It is important to take the full course of antibiotic therapy even when symptoms are gone to make sure the antibiotic completely eliminates the strep bacteria. Possible complications of strep throat, which are more likely to occur with delayed treatment or in untreated strep throat, are serious and include PERITONSILLAR ABSCESS, GLOMERULONEPHRITIS (strep infection involving the KIDNEYS), and rheumatic heart disease (strep infection involving the HEART valves).

Risk Factors and Preventive Measures

Strep throat is most common in children between the ages of 5 and 15, though people of any age may acquire the infection. People who have their tonsils have greater risk. Diligent PERSONAL HYGIENE; frequent HAND WASHING; and avoiding the sharing of drinks, foods, and eating utensils among family members or friends are measures that can reduce the risk for exposure to the strep bacteria.

See also ANTIBIOTIC RESISTANCE; MENINGITIS; SCARLET FEVER; TOXIC SHOCK SYNDROME.

syphilis A sexually transmitted disease (STD) that results from INFECTION with the bacterium *Treponema pallidum*. Syphilis spreads through vaginal intercourse, anal intercourse, and oral sex. It is not possible to acquire syphilis from objects such as toilet seats or in hot tubs. Syphilis is curable with appropriate antibiotic therapy. Untreated syphilis can cause widespread damage in the body. Congenital syphilis, which a pregnant woman who has syphilis can pass to her unborn child, can cause numerous abnormalities or STILLBIRTH.

Symptoms and Diagnostic Path

Untreated syphilis has four stages: primary, secondary, latent, and tertiary. Symptoms are specific to the stage of illness. Diagnosis typically occurs through BLOOD tests that confirm the presence of antibodies or examination of cell samples (such as from body fluids) under a microscope that reveal the presence of *T. pallidum* BACTERIA.

Primary syphilis Primary syphilis is the first manifestation of illness and occurs two to six weeks after infection with *T. pallidum*. Its symptom is the formation of a painless, ulcerlike sore (chancre) at the site where the infection entered the body. Because this site may be inside the VAGINA in a woman or within the URETHRA in a man, the chancre often goes undetected and heals.

Secondary syphilis Though the chancre heals the *T. pallidum* bacteria continue to multiply and invade the blood circulation, which carries them throughout the body. The characteristic symptoms of secondary syphilis emerge about two months after the chancre and include

- skin RASH of brown spots or sores that involves the palms of the hands and soles of the feet as well as other locations on the body
- mucous patches in the vagina or MOUTH and on the PENIS
- condylomata lata, which are spongy, wartlike patches that often appear on the labia (women) or SCROTUM (men)
- low-grade FEVER (around 100°F)
- sore THROAT and HEADACHE

Secondary syphilis lasts up to three months, during which the person can spread the infection to others through nonsexual as well as sexual contact because the sores of the rash contain *T. pallidum* bacteria. Some people experience outbreaks of secondary syphilis symptoms for a year or longer.

Latent syphilis In latent syphilis the bacteria remain in the body but cause no symptoms. During this stage the person cannot pass the infection to other people. Latent syphilis may last for decades, during which the bacteria silently attack the NERVOUS SYSTEM, joints, HEART, and other structures.

Tertiary syphilis The last stage of syphilis, the tertiary stage, is the emergence of symptoms resulting from the damage that occurred during the latent stage. Damage is often widespread and significant, producing symptoms of cognitive dysfunction, blindness, heart disease, kidney disease, and NEUROPATHY (sometimes called neurosyphilis).

Treatment Options and Outlook

Treatment for syphilis at any stage is penicillin by injection (or doxycycline for people who are allergic to penicillin). Most people who receive treatment for primary or secondary syphilis recover completely. Treatment can still cure tertiary syphilis but the damage the infection has already caused is permanent. Reinfection is possible; there is no IMMUNITY for syphilis. All sexual partners should be tested so they can receive treatment if they have syphilis. Primary syphilis carries increased risk for HIV infection because the chancre gives an easy pathway for the VIRUS to enter the body.

Risk Factors and Preventive Measures

People who have multiple sexual partners and men who have sex with men have the greatest risk for contracting syphilis and other STDs. Precautions such as condom use with all sexual activity reduce the risk for infection. Early diagnosis and treatment are essential to prevent complications and to prevent spreading the infection to other people.

See also CHLAMYDIA; GENITAL HERPES; GONORRHEA; HUMAN PAPILLOMAVIRUS (HPV); SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SEXUALLY TRANSMITTED DISEASES (STDS).

T

toxic shock syndrome A systemic IMMUNE RESPONSE to the endotoxins many BACTERIA produce during infections. The immune response produces widespread, significant INFLAMMATION involving multiple organ systems. Staphylococcal toxic shock syndrome, resulting from *Staphylococcus aureus* INFECTION, is more common and causes milder illness. Streptococcal toxic shock syndrome, which results from group A beta-hemolytic streptococcal bacteria, produces severe illness and causes death in about 60 percent of people who develop it.

Symptoms are those of acute bacterial infection such as FEVER and PAIN, with HYPOTENSION (low BLOOD PRESSURE) and RASH that involves the entire body, including the palms of the hands and soles of the feet. Illness is severe enough to require hospitalization, often in an intensive care unit, for supportive medical care (including fluid replacement, cardiovascular stabilization, and MECHANICAL VENTILATION as necessary) and treatment with intravenous IMMUNOGLOBULIN and ANTIBIOTIC MEDICATIONS. Complications of toxic shock syndrome are potentially life-threatening and include DISSEMINATED INTRAVASCULAR COAGULATION (DIC), ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS), and NECROTIZING FASCIITIS. People who recover from toxic shock syndrome may have lingering health problems and are at risk for RECURRENCE.

Toxic shock syndrome first emerged as a significant health issue in the 1980s when superabsorbent tampons new on the market caused an outbreak of toxic shock syndrome among otherwise healthy women. The superabsorbency of the tampons meant women could change them less frequently, an unexpected SIDE EFFECT of which was a spike in bacterial infections. Changes in tampon materials and widespread education efforts have significantly reduced toxic shock syndrome due to tampon use, although tampon use remains a risk factor. Other risks for toxic shock syndrome include surgical packing (such as after an OPERATION on the NOSE) and illness due to common bacterial infections.

See also SCARLET FEVER; STREP THROAT; SEPTICEMIA.

toxoplasmosis An illness that results from INFECTION with the PARASITE *Toxoplasma gondii*. Health experts in the United States estimate that about 60 million Americans are infected with *T. gondii,* though only a small percentage of them become ill. *T. gondii* may migrate into body tissues, forming cysts.

Domestic cats carry *T. gondii*; cat feces in litter boxes and outdoors in garden areas are the most common source of infection. Outdoor cats are more likely to have *T. gondii*. Other sources of *T. gondii* include undercooked or raw meats, especially pork and lamb. People acquire the infection through touching contaminated objects and then transmitting the parasites to food or drink. Children may acquire *T. gondii* infection through playing in outdoor sandboxes.

Toxoplasmosis is often an OPPORTUNISTIC INFECTION that causes illness in people who are IMMUNOCOMPROMISED, such as people who have HIV/AIDS or who are taking IMMUNOSUPPRESSIVE THERAPY after ORGAN TRANSPLANTATION. Toxoplasmosis, whether or not it produces symptoms, is a particular risk for a pregnant woman because she can pass the infection to her unborn child. The cysts that *T. gondii* form in the tissues can cause serious BIRTH DEFECTS in the developing fetus, including damage to the eyes that results in permanent loss of vision. HEARING LOSS and neurologic injuries are also common.

Symptoms, when they occur, are similar to those of influenza and may include

- FEVER
- MUSCLE aches and JOINT PAIN
- upper respiratory congestion
- tiredness or fatigue

A BLOOD test that shows the presence of antibodies confirms the diagnosis. Anyone who has ever had toxoplasmosis will have a positive blood test; infection confers lifelong IMMUNITY. Toxoplasmosis is self-limiting; once the illness runs its course any symptoms subside. Though the *T. gondii* remain in the body, the IMMUNE SYSTEM can contain them so they do not cause illness. Doctors may recommend treatment with sulfadoxine and pyrimethamine, two medications used to prevent MALARIA, for pregnant women who acquire *T. gondii* infection or develop toxoplasmosis and for people who are immunocompromised. These medications are effective because *T. gondii* is similar to the parasite that causes malaria. The antibiotic clindamycin is also effective in people who are immunocompromised.

Washing the hands with warm water and soap after handling cats, cleaning litter boxes, gardening, and preparing pork or lamb removes *T. gondii*, preventing infection. Pregnant women should also wear gloves when gardening or cleaning litter boxes.

See also ANTIBIOTIC MEDICATIONS; HAND WASHING; INVESTIGATIONAL NEW DRUG (IND).

transmission modes The methods by which pathogens spread to cause INFECTION. Common transmission modes include

- airborne, in which pathogens enter the respiratory tract as particles suspended in the air
- sexual, in which pathogens enter the body through sexual contact
- direct contact, in which pathogens enter the body via touch
- foodborne, in which consumed foods contain pathogens
- waterborne, in which consumed water and foods prepared in that water contain pathogens
- bloodborne, in which pathogens enter the blood circulation through BLOOD TRANSFUSION or contaminated needles

Many infectious agents have multiple transmission modes. The common cold, for example, spreads through direct contact with nasal secretions as well as via airborne droplets.

See also COLDS; FOODBORNE ILLNESSES; PATHOGEN; SNEEZE/COUGH ETIQUETTE; WATERBORNE ILLNESSES.

trichomoniasis A sexually transmitted disease (STD) resulting from INFECTION with the protozoan *Trichomonas vaginalis*. Though trichomoniasis affects men and women equally, women are more likely to show symptoms. About two thirds of men and half of women who have trichomoniasis do not have symptoms, though they are nonetheless able to spread the infection through sexual contact.

Symptoms of trichomoniasis include

- greenish or yellowish, often foul-smelling, discharge
- lower abdominal discomfort
- in men, burning with URINATION
- in women, vaginal or vulvar itching or burning

The diagnostic path includes examination under the microscope of a sample of the discharge, which usually contains *T. vaginalis* though a third of people who have the infection may have negative findings with this test. Culture of discharge samples can provide definitive diagnosis. Treatment is oral therapy with the medication metronidazole. It is important to also treat all sexual partners, as the likelihood that they also have the infection is very high. Appropriate treatment cures trichomoniasis, though infection may recur with reexposure. Without treatment the infection remains active. Complications of untreated trichomoniasis include EPIDIDYMITIS and PROSTATITIS in men and chronic vaginitis and vaginal ulcerations in women.

See also CANDIDIASIS; CHLAMYDIA; GENITAL HERPES; GONORRHEA; HUMAN PAPILLOMAVIRUS (HPV); SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SEXUALLY TRANSMITTED DISEASES (STDS); SYPHILIS; URETHRITIS.

tuberculosis An illness resulting from INFECTION with the MICROBE *Mycobacterium tuberculosis*. Though tuberculosis most commonly infects the LUNGS, the disease may involve other organs as well, notably the KIDNEYS. Health experts estimate more than 2 billion people worldwide have active (symptoms are present) or latent (symptoms are not present) tuberculosis. An important characteristic of mycobacteria is their ability to rapidly develop resistance to ANTIBIOTIC MEDICATIONS.

Untreated tuberculosis is debilitating and progressive, giving the appearance that it consumes the body. This characteristic accounts for the archaic common name of the disease, "consumption." Tuberculosis was a leading cause of death throughout the world until the discovery of the FUNGUS-derived antibiotic streptomycin in 1944. Today's treatment regimens seldom incorporate streptomycin, however, because of its high likelihood for causing HEARING LOSS (OTOTOXICITY) and because many strains of *M. tuberculosis* have developed resistance to it.

When breathed into the lungs, *M. tuberculosis* BACTERIA infect macrophages, white BLOOD cells responsible for consuming invading pathogens, in the alveoli. Rather than the MACROPHAGE consuming the *M. tuberculosis* bacterium, however, the bacterium takes over the macrophage. Other cells of the IMMUNE RESPONSE surround the infected macrophage, enclosing it within a GRANULOMA. The bacteria may remain dormant within the granuloma. When enough granulomas accumulate, they interfere with the normal function of the organ—typically the lungs, though also the kidneys, bones, and BRAIN when *M. tuberculosis* bacteria migrate to those structures.

Symptoms and Diagnostic Path

Many people who have tuberculosis do not have symptoms and do not know they have the infection. Chest X-RAY for other diagnostic reasons may detect lesions in the lungs; other people learn they have tuberculosis through routine tuberculin SKIN testing such as many states in the United States require for people who work with the public, such as health-care workers and food service workers. When symptoms are present they include

- prolonged, productive COUGH that may include blood (HEMOPTYSIS)
- unintended weight loss
- FEVER
- night sweats
- fatigue
- wheezing or feeling of tightness in chest

The diagnostic path includes chest X-ray, tuberculin skin test, and cultures of sputum samples. When the findings of these diagnostic procedures are inconclusive, the doctor may conduct additional tests, including BRONCHOSCOPY or COMPUTED TOMOGRAPHY (CT) SCAN.

Treatment Options and Outlook

Current treatment regimens use multiple medications in a rotating pattern over 9 to 12 months. The first phase of treatment—the initial phase, which lasts two months—generally involves taking four medications. The second phase of treatment—the continuation phase, which lasts four to seven months—generally incorporates a combination of two medications. The specific drugs depend on numerous clinical factors, including the person's HIV status and the sensitivities of the causative strain of *M. tuberculosis* from sputum cultures.

MEDICATIONS TO TREAT TUBERCULOSIS

Standard Infection	
ethambutol	isoniazid
pyrazinamid	rifabutin
rifampin	rifapentine
Resistant Infection	
amikacin	capreomycin
cycloserine	ethionamide
gatifloxacin	kanamycin
levofloxacin	moxifloxacin
p-aminosalicylic acid	protionamide
pyrazinamide	viomycin

Symptoms in most people improve dramatically within three weeks of starting medication, though clinical changes (X-ray) often do not become apparent for several months. Treatment regimens are complex, and the medications can cause unpleasant side effects, the combination of which tempts people to stop taking the medications.

Doing so is hazardous both for the person, who then remains infected with tuberculosis, and in the context of public health because it fosters DRUG resistance. It is essential to take the medications as directed for the full course of treatment. When compliance is a significant concern, doctors may use a protocol called directly observed treatment (DOT), in which the person comes to a clinic and takes his or her medication under direct observation of a health-care provider. Such treatment cures the tuberculosis. Any damage to the lungs or the kidneys (granulomas) remains, however, and is permanent.

Risk Factors and Preventive Measures

Crowded, unsanitary living conditions present the greatest risk for tuberculosis infection. Active tuberculosis is contagious through contact with sputum (material coughed up from the lungs), which contains *M. tuberculosis*. Latent tuberculosis is not contagious, though may emerge as active disease and become contagious. Tuberculosis is a common OPPORTUNISTIC INFECTION in people who have HIV/AIDS. Prevention efforts focus on routine testing of people at risk for exposure. In the United States, such testing takes place through public health programs, school-based programs, institutional programs (such as in the military and in prisons), and employer-based programs. People who have positive skin tuberculin tests should receive further evaluation from a doctor and may require a course of prophylactic treatment with anti-tuberculosis medications.

See also BONE; COMMUNITY SANITATION; PATHOGEN.

typhoid fever An illness resulting from INFECTION with the bacterium *Salmonella typhi*. Typhoid FEVER is rare in the United States, and most people who have the illness acquire the infection while traveling in regions of the world where typhoid fever is endemic. Substandard COMMUNITY SANITATION is the key risk for the spread of typhoid fever. The BACTERIA infect the SMALL INTESTINE. Infection spreads through fecal–oral contamination, primarily through consumption of contaminated water and foods. Some people are carriers of typhoid fever; they are infected with *S. typhi* but do not develop symptoms or illness.

Symptoms of typhoid fever include

- high fever
- NAUSEA, VOMITING, and DIARRHEA
- RASH
- ABDOMINAL PAIN
- extreme fatigue and weakness

Cultures of BLOOD and stool samples reveal the presence of *S. typhi*, which is conclusive for diagnosis. Treatment is ANTIBIOTIC MEDICATIONS, commonly ampicillin, trimethoprim-sulfamethoxazole (TMP-SMZ), or ciprofloxacin. Most people feel much improved within three days of starting antibiotic therapy, though the bacteria may remain in their bodies for six weeks or longer, during which time they remain contagious (capable of passing the infection to others). People who work in food service, health care, and other public contact jobs may require a doctor's statement of health, verifying negative blood and stool cultures, before they can return to work. People who are planning to travel to regions of the world where typhoid fever is common should receive typhoid fever VACCINE to prevent infection.

See also FOODBORNE ILLNESSES; WATERBORNE ILLNESSES.

V–W

virus An infectious PATHOGEN that must invade a host cell to replicate, technically called an obligate intracellular PARASITE. A virus is a particle of living material that contains an inner core of nucleic acid (DNA or RNA), called the genome, encased in an outer shell of protein, called a capsid. Some viruses contain a third layer composed of lipids, called an envelope, that further protects and nourishes the virus. These components, collectively called a virion, cannot themselves support a full life cycle, which obligates the virus to find a host to maintain its survival. A virus can attach only to the type of cell capable of supporting it, binding to specific protein molecules on the surface of the cell membrane.

ANTIBIOTIC MEDICATIONS are not effective in treating illnesses that result from viral infections, such as COLDS and INFLUENZA.

After invading a host cell, a virus hijacks the cell's structures and functions to serve its own needs and to replicate itself. DNA viruses produce

COMMON VIRUSES AND THE ILLNESSES THEY CAUSE

Virus or Viral Family	Genetic Configuration	Illness
ADENOVIRUS	DNA	PHARYNGITIS, PNEUMONIA, acute respiratory disease, cervicitis, URETHRITIS, CYSTITIS, GASTROENTERITIS
CYTOMEGALOVIRUS (CMV)	DNA	CMV INFECTION
EPSTEIN-BARR VIRUS	DNA	infectious mononucleosis, Burkitt's lymphoma, Hodgkin's lymphoma
HEPATITIS A virus (HAV), hepatitis C virus (HBV)	RNA	HEPATITIS
HERPES SIMPLEX virus 1 (HSV-1)	DNA	COLD SORE
herpes simplex virus 2 (HSV-2)	DNA	GENITAL HERPES
human herpesvirus 8 (HHV-8)	DNA	KAPOSI'S SARCOMA
human immunodeficiency virus 1 (HIV-1), human immunodeficiency virus 2 (HIV-2)	RNA retrovirus	AIDS

Virus or Viral Family	Genetic Configuration	Illness
human papillomavirus (HPV)	DNA	genital WARTS, CERVICAL CANCER, vaginal cancer
human parainfluenza viruses	RNA	acute upper respiratory disease, CROUP, bronchiolitis, BRONCHITIS, pneumonia
INFLUENZA viruses	RNA	influenza (flu)
MEASLES virus	RNA	measles
MUMPS virus	RNA	mumps
Norwalk-like viruses	RNA	acute gastroenteritis
poliovirus	RNA	POLIOMYELITIS
RABIES virus	RNA	rabies
respiratory syncytial virus	RNA	bronchiolitis, pneumonia, acute upper respiratory disease
rhinoviruses	RNA	COLDS
RUBELLA virus	RNA	rubella (German or three-day measles)
varicella-zoster	DNA	CHICKENPOX, HERPES ZOSTER (shingles)
variola	DNA	SMALLPOX

proteins that the host cell's RNA transcribe as instructions to replicate the virus's DNA, which the cell does. DNA contains the instructions for the cell's functions; RNA forms the messenger proteins that carry out the directives of the DNA. Eventually the virus's copies of DNA crowd out the cell's copies of DNA, and the cell becomes the agent of the virus. The cell either divides or ruptures, spreading the virus. RNA viruses achieve a similar result by causing the host cell to replicate their RNA, which then replaces the cell's RNA. Retroviruses are RNA viruses that contain the enzyme reverse transcriptase, which allows RNA to instruct DNA (the reverse of normal).

Viruses are highly adaptable and have numerous mechanisms to hide from the IMMUNE SYSTEM, allowing them to become well established infections before the immune system detects their presence. Once the immune system does detect a virus, it develops antibodies that protect against subsequent infection by the same virus. Many common viruses—such as those that are responsible for COLDS (rhinoviruses), GASTROENTERITIS (enteroviruses), and the flu (INFLUENZA viruses)—frequently alter their structures, evolving into different strains that can cause the same illnesses. Some viruses, such as human T-lymphotropic virus (HTLV) and HUMAN PAPILLOMAVIRUS (HPV), cause cancer (oncoviruses). The human immunodeficiency virus (HIV) is a retrovirus that attacks the immune system, causing AIDS (acquired immunodeficiency syndrome).

See also ANTIBODY; ANTIBODY-MEDIATED IMMUNITY; CELL-MEDIATED IMMUNITY; HIV/AIDS.

waterborne illnesses Diseases that result from pathogens transmitted by drinking or otherwise consuming contaminated water. Heavy metals and

industrial chemicals may also contaminate water supplies, causing poisoning. People may acquire waterborne infections through drinking water supplies or by swallowing water during recreational activities in lakes, rivers, pools, hot tubs, and similar sources.

Drinking water supplies in the United States must meet established DRINKING WATER STANDARDS for purity, which state and local health departments monitor through regular and spontaneous testing. Water that does not come from a community water supply or properly maintained and disinfected private well should be boiled for one minute, then cooled, before drinking or using to prepare food.

Environmental water sources such as lakes and rivers contain numerous BACTERIA and parasites that can cause illness with contact or consumption. Contamination is higher after steady or heavy rain, as runoff water that drains into streams, rivers, and lakes is likely to contain animal excrement as well as soil-based microbes. Recreational activities such as boating, swimming, water-skiing, and fishing hold increased risk for exposure to such pathogens. It is important to avoid swallowing environmental water and to shower to rinse the SKIN after being in the water. People who hike and camp in back-country areas should use appropriate decontamination or filtration methods to draw drinking water from natural sources. A rapidly moving stream or river does not necessarily contain fewer microbes, and the clearness of water's appearance does not mean it is safe to drink.

COMMON WATERBORNE ILLNESSES

CRYPTOSPORIDIOSIS	*Escherichia coli* INFECTION
GIARDIASIS	HEPATITIS A
AMEBIASIS	CYCLOSPORIASIS
CAMPYLOBACTERIOSIS	SALMONELLOSIS
SHIGELLOSIS	viral GASTROENTERITIS

See also COMMUNITY SANITATION; ENVIRONMENTAL HAZARD EXPOSURE; FOODBORNE ILLNESSES; FOOD SAFETY; HEAVY-METAL POISONING; HEPATITIS PREVENTION; PARASITE; POISON PREVENTION.

CANCER

The area of health care concerned with cancer prevention and treatment is oncology. Doctors who specialize in cancer treatment are oncologists. This section, "Cancer," presents an overview discussion of current understanding about cancer and entries about cancer concepts and treatments. Entries in other sections of The Facts On File Encyclopedia of Health and Medicine *provide detailed content about specific types of cancer.*

For example, this section, "Cancer," contains the entry HORMONE-DRIVEN CANCERS, whereas while the section "The Reproductive System" contains entries for BREAST CANCER, PROSTATE CANCER, and TESTICULAR CANCER. Cross-references connect entries with one another.

Cancer: Uncontrolled Cell Proliferation

Cancer is the uncontrolled growth and division (proliferation) of cells. Cancer cells lack the proper mechanisms for APOPTOSIS, the natural process that establishes the end of a cell's life cycle. In this regard, cancer cells have an endless open throttle: they can divide forever. Cancer cells also lack the proper mechanisms for self-regulation that shut down cell division in abnormal cells; they never stop growing and dividing.

Ordinarily the IMMUNE SYSTEM detects cells that present a threat to the body and mobilizes an IMMUNE RESPONSE to neutralize them before they can do much damage. Cancer cells appear able to evade such detection by the immune system because they arise from cells that belong to the body (self cells). Even as they mutate cancer cells retain enough essence of their self-cell origin to fool the immune system into continuing to perceive them as self cells. This deception allows cancer cells to congregate, forming the tumors that characterize the disease process of cancer.

Cancer may develop in any cell, with the potential to affect any kind of body tissue. The cells form tumors that invade healthy tissues and can spread to parts of the body beyond the site of origin. Cancer is a threat to health because its presence within tissues and organs disrupts their structure and functions. Cancer tumors take space, NUTRIENTS, and structure that tissues and organs need.

Heredity, Environment, and Aging

Researchers believe cancer is the result of genetic damage within individual cells that allows uncontrolled cell division and growth. This damage may occur as a consequence of heredity or environment or may develop through the process of aging.

Heredity and cancer The tendency toward cancer appears to run in families, providing much anecdotal evidence of genetic mutations that contribute to the risk for cancer. Researchers also have isolated specific genes for certain types of cancer, providing objective evidence that cancer can have a hereditary component. When this is the case, a person inherits mutated genes that do not properly regulate specific functions. This lack of regulation results in abnormal cell growth and division that can result in cancer. The BRCA-1/BRCA-2 GENE mutations are among the best known; these mutations are prominent in women who have some types of OVARIAN CANCER or breast cancer. However, only a small percentage of women who have these gene mutations develop cancer, evidence that many factors converge when cancer occurs.

Environmental influences and cancer More than a thousand substances found in the environment, natural and synthetic, may cause cancer.

Most are chemicals or sources of radiation, both of which alter the molecular structure of cells in ways that change their functions. The most common natural CARCINOGEN is the ultraviolet radiation of sunlight, which is responsible for nearly all SKIN CANCER. Other carcinogens are manmade, notably industrial chemicals such as formaldehyde and vinyl chloride. Many manufacturing processes use these and other carcinogenic chemicals; it is nearly impossible to avoid exposure to them.

Aging and cancer Genetic damage to cells may also occur as a consequence of natural deterioration within cells that takes place with aging. Cells become less able to repair themselves and exposure to carcinogens leaves them more vulnerable, allowing errant growth and division. Some cancers that are more common in advanced age are also less harmful to health overall. For example, researchers estimate that 90 percent of men over age 85 have prostate cancer, yet in most of them the cancer is so slow growing that it does not require treatment.

Traditions in Medical History

Surgery was the first treatment for cancer. Even ancient documents record procedures for removal of tumors. However, the development of ANESTHESIA gave surgery its big boost as treatment for cancer, allowing surgeons to more selectively remove cancerous tumors. Though the operations were often extensive and traumatic, they were able to save lives.

RADIATION THERAPY was the next treatment developed for cancer. Though doctors began using X-rays on tumors shortly after the discovery of X-rays in the late 19th century, the treatment was often more dangerous than the cancer. Radiation BURNS and radiation sickness were common as doctors struggled to find a balance between enough radiation to kill the tumor and not enough radiation to kill the patient. Finally, in the middle of the 20th century advances in technology and understanding made it possible for radiation to achieve this balance.

For centuries folk medicine contained various substances purported to treat cancer, some of which have become the basis for contemporary CHEMOTHERAPY (such as the camptothecins, vinca alkyloids, and taxanes). During the first half of the 20th century doctors realized that one SIDE EFFECT of poisonous mustard gas, used as a weapon of war, was that it eradicated certain types of cancer. Further exploration resulted in the first class of therapeutic chemotherapy agents, the alkylating agents.

In the later decades of the 20th century, researchers made significant breakthroughs in understanding the functions of the immune system and were able to develop methods to take advantage of the body's own mechanisms for fighting cancer. IMMUNOTHERAPY is now at the forefront of cancer research.

Breakthrough Research and Treatment Advances

Cancer treatment focuses on removing or disabling cancer cells so they can no longer grow and divide. Though cancer remains the second-leading cause of death in the United States, successes in treatments since the 1990s have improved the outlook significantly. Nearly 10 million Americans live with their cancer under control, in REMISSION, or cured. Treatment is so often curative for basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), the two most common types of SKIN cancer, that cancer statistics do not include these cancers among them.

As researchers learn more about cancer, they are discovering ways to bolster the immune system's ability to detect and eradicate cancer cells before they gain enough momentum to establish themselves as tumors. Cancer vaccines currently in investigational trials show great promise for preventing the development of CERVICAL CANCER, prostate cancer, and lymphoma, and for preventing the RECURRENCE of other types cancer. New treatments specifically target molecular functions, either in cancer cells or within the immune response. These therapies reduce the unpleasant side effects traditionally characteristic of cancer treatment as well as improve the ability to eradicate the cancer. Other therapies establish boundaries around the cancer, containing it so it cannot spread and interfere with structures and functions. Many types of cancer may soon be as manageable (and perhaps preventable) through therapeutic interventions and lifestyle modifications as other chronic health conditions such as CARDIOVASCULAR DISEASE (CVD) and DIABETES.

A–B

adenocarcinoma A type of cancer that arises from the endothelial cells of glandular structures. Adenocarcinoma is the most common type of cancer to occur in the PROSTATE GLAND (PROSTATE CANCER), gastrointestinal tract (ESOPHAGEAL CANCER, STOMACH CANCER, PANCREATIC CANCER, LIVER CANCER, COLORECTAL CANCER), and endocrine glands (TESTICULAR CANCER, OVARIAN CANCER, THYROID CANCER). Adenocarcinoma begins as a benign (noncancerous) tumor, an adenoma. Over time, GENE mutations in the cells of the adenoma may cause the tumor to transition to an adenocarcinoma. Adenocarcinomas can involve numerous organs and tissues.

See also BLASTOMA; CARCINOMA; ENDOCRINE GLAND; FAMILIAL ADENOMATOUS POLYPOSIS (FAP); HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC); INTESTINAL POLYP; LEUKEMIA; MUTATION; SARCOMA.

adenoma-to-carcinoma transition The changes that take place in an ADENOMA, a benign (noncancerous) tumor, as it transforms into an ADENOCARCINOMA, a malignant (cancerous) tumor. The transition to cancer can occur with any adenoma though is most common with adenomas of the colon (intestinal polyps, also called adenomatous polyps). Only a small percentage of adenomas become cancerous. The sequence of events that transform an adenoma to an adenocarcinoma begins with multiple mutations in the genes that regulate cell division and APOPTOSIS (planned cell death). Over a series of cell divisions the mutations become increasingly prevalent among the cells, resulting in DYSPLASIA and ultimately cancer. Because of the risk for an adenoma to become adenocarcinoma, doctors often surgically remove adenomas when feasible.

See also CANCER PREVENTION; COLORECTAL CANCER; FAMILIAL ADENOMATOUS POLYPOSIS (FAP); GENE; HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC); INTESTINAL POLYP; MUTATION.

adult survivors of childhood cancer The current generation of adults is the first to grow up in the era of successful treatment for many childhood cancers. Nearly 300,000 American adults who are now in their 20s, 30s, and 40s enjoy CANCER-free, healthy lives. Doctors consider treatments for most types of LEUKEMIA, the most common childhood cancer, to be curative. Treatments for many types of BONE CANCER, BRAIN cancer, Hodgkin's LYMPHOMA, and kidney cancer (WILMS'S TUMOR) are also curative. Some health concerns may linger or occur, however, as a result of the cancer itself or the therapies used to treat the cancer.

Complications of Cancer Treatment

Complications of cancer treatment are the most significant cause of later health concerns for adults who had cancer as children. Some therapies for cancer that were the standard of care 20 or 30 years ago presented significant health risks that survivors are now beginning to experience. For example, doctors now know the CHEMOTHERAPY drugs, notably anthracyclines such as doxorubicin, can cause HEART FAILURE that tends to show up 10 to 30 years after treatment. Chemotherapy drugs affect all rapidly dividing cells in the body and can have a significant effect on healthy cells notably in the endocrine system, affecting THYROID GLAND function, growth, PUBERTY, and FERTILITY. Radiation to the chest, such as to treat lymphoma, can damage the HEART, manifesting in adulthood as CARDIOMYOPATHY or heart failure. Radiation to the head

or EYE can result in vision and hearing problems. Surgery, particularly AMPUTATION, may result in lifelong health issues that require regular medical attention.

Increased Risk for Another Cancer

Having had cancer increases the risk for developing another cancer later in life. For this reason, regular health screening for cancer is especially important for adults who had cancer as children. Radiation therapy and chemotherapy both increase the risk for leukemia and lymphoma, likely as a consequence of damage to the bone marrow during cancer treatment and especially chemotherapy. Radiation therapy to the upper body raises the risk for lung cancer, particularly when other risk factors for lung cancer exist such as cigarette smoking, and for breast cancer in women.

Emotional Health

The emotional consequences of successful cancer treatment in childhood may be pervasive, with numerous effects people do not recognize as related to the cancer experience. Some studies show that adults who had cancer as children reexperience the range of emotions and fears that accompanied their cancer when as adults they enter medical environments for health care of any kind, often as a presentation of POST-TRAUMATIC STRESS DISORDER (PTSD). The reaction to the current situation may be out of proportion to the situation itself. Having survived a health crisis as serious as cancer as a child may have a profound effect on a person's ability to engage in activities of life, manifesting as withdrawal in some people and in high-risk behaviors in others.

Maintaining a Balanced Perspective

It is important for adults who had cancer as children to maintain a balance between diligence and confidence when it comes to health matters. More often than not, subsequent health concerns arising from childhood cancer or its treatment are treatable and manageable, particularly with early detection. Many cancer treatment centers now offer follow-up services, including counseling, for adult survivors of childhood cancer.

See also CANCER PREVENTION; CANCER RISK FACTORS; LIFESTYLE AND CANCER.

alternative and complementary remedies for cancer Therapies outside the realm of conventional medical methods that are promoted to relieve cancer symptoms. Alternative practices are used instead of conventional treatments and methods; complementary practices are used in conjunction with conventional treatments and methods. Some therapies and remedies may be either alternative or complementary, depending on how they are used. Because some cancer treatment protocols are very precise, it is important to discuss alternative and complementary approaches with the oncologist before using them.

Complementary Therapies

Complementary therapies are often effective for treating symptoms related to cancer and discomforts related to conventional cancer treatment. ACUPUNCTURE, BIOFEEDBACK, and HYPNOSIS can provide relief from PAIN and NAUSEA. YOGA, TAI CHI, and MEDITATION provide relaxation and stress relief. Some therapies, such as acupuncture and biofeedback, have undergone clinical research studies that support their effectiveness and usefulness. Most complementary therapies integrate well with conventional treatments. Some herbal remedies, such as products for nausea or relaxation, may interact with chemotherapy drugs.

Alternative Remedies

Alternative remedies for cancer are approaches to treat cancer that have not been proven effective through conventional research studies; some have been proven ineffective. Alternative therapies may include health-care systems that differ in philosophy and practice from conventional Western medicine, such as AYURVEDA, HOMEOPATHY, and TRADITIONAL CHINESE MEDICINE (TCM). Alternative remedies may also consist of conventional treatments used in unproven or disproven ways; most have either not been subjected to conventional research study or have been disproved. Some alternative remedies are potentially harmful in themselves as well as for the delay they may cause

in receiving conventional treatments that could have health benefits.

Making Choices and Decisions

Choices and decisions in regard to treatment for cancer are not easy to make, particularly when the diagnosis comes after the cancer is fairly advanced or has metastasized. Emotions are high, and sometimes the route of conventional treatment has little to offer beyond palliative care. Alternative remedies may make claims that sound too good to pass up. Cancer experts urge people to fully explore the remedy and the evidence that surrounds its usefulness. These key questions can help put the claims of the therapy or remedy in perspective:

- What does the remedy do—specifically? How does it affect the cancer?
- Does the remedy claim to be able to replace or support medical treatments?
- Who administers or provides the remedy?
- What are the remedy's possible side effects?
- What kinds of research have tested the remedy?
- What is the cost of the remedy?
- Is the remedy available in the United States?

Unfortunately, many purported cancer remedies are ineffective at best and potentially harmful. In some circumstances those who are marketing the remedy sincerely believe in its ability to treat or even cure cancer. However, the market for alternative remedies also offers abundant opportunity for fraud. Complementary therapies that supplement conventional treatment can provide comfort and relief from many symptoms related to cancer and cancer treatment. Choosing an ineffective alternative remedy in lieu of conventional treatment may have irreversible consequences for health and for QUALITY OF LIFE.

An oncologist or credentialed cancer care center can provide information and guidance for choosing complementary therapies that are helpful. The Web sites for the American Cancer Society (www.cancer.org), the US National Cancer Institute's Office of Cancer Complementary and Alternative Medicine (www.cancer.gov/cam), and the US National Center for Complementary and Alternative Medicine (nccam.nih.gov) provide current information about alternative remedies and complementary therapies for cancer.

See also CHEMOTHERAPY; COPING WITH CANCER; DIAGNOSING CANCER; RADIATION THERAPY; SURGERY FOR CANCER.

angiogenesis inhibitor drugs Substances that stop tumors from developing new BLOOD vessels to support their survival. Numerous proteins and enzymes in the body function to encourage or suppress the growth of new blood vessels. Cancerous tumors are among the tissues that produce proteins that foster new blood vessel growth; these blood vessels then deliver to the tumor the nourishment it needs to grow. Cutting off the blood supply starves the tumor, causing its cells to die.

Among the natural angiogenesis inhibitors in the body are the INTERFERONS, which doctors have used in therapeutic forms with some success to slow tumor-related blood vessel growth. Some CHEMOTHERAPY drugs also have a secondary antiangiogenesis effect. In 2004 the US Food and Drug Administration (FDA) approved the first DRUG specifically developed to block angiogenesis, a monoclonal antibody that is called bevacizumab (Avastin).

Angiogenesis inhibition is of therapeutic interest in health conditions other than cancer that result from overgrowth of blood vessels, such as AGE-RELATED MACULAR DEGENERATION (ARMD) and RETINOPATHY of DIABETES. Research into drugs to encourage angiogenesis to restore blood flow to the HEART after HEART ATTACK or in severe ISCHEMIC HEART DISEASE led to many advances in angiogenesis inhibition as well.

See also CELL STRUCTURE AND FUNCTION; MOLECULARLY TARGETED THERAPIES; MONOCLONAL ANTIBODIES (MABS); TRANSMYOCARDIAL LASER REVASCULARIZATION (TMLR).

blastoma A cancerous tumor that arises from the immature cells that form the basis for an organ's structure. The cells are undifferentiated, which means they have not yet developed a specific role within the body. Researchers believe these are embryonic cells. Blastomas grow as the

type of tissue where the embryonic cells remain after organ development. Blastomas nearly always occur in childhood, though occasionally may occur in early adulthood. Most blastomas are malignant (cancerous), though osteoblastoma (blastoma of the BONE) is a benign (noncancerous) tumor. Treatment for blastoma typically combines surgery to remove the tumor with CHEMOTHERAPY, RADIATION THERAPY, or both to shrink the tumor before surgery and destroy any lingering cancer cells after surgery. The precise combination depends on the tumor's location and size at the time of diagnosis.

TYPES OF BLASTOMA

Tumor	Location
medulloblastoma	BRAIN
nephroblastoma	kidney
RETINOBLASTOMA	RETINA of the EYE
osteoblastoma	BONE
neuroblastoma	NERVOUS SYSTEM tissue
glioblastoma multiforme (GBM)	brain

See also ADENOCARCINOMA; CARCINOMA; LEUKEMIA; SARCOMA; SURGERY FOR CANCER; SURGERY BENEFIT AND RISK ASSESSMENT; WILMS'S TUMOR.

BRCA-1/BRCA-2 BREAST CANCER GENE 1 and breast cancer gene 2, the first genes in which researchers identified mutations that correlate to increased susceptibility to BREAST cancer and OVARIAN CANCER. About one in six women who have either of these cancers have mutations in either or both of the genes. Many are women who have a known family history of breast cancer or ovarian cancer. The presence of mutations in either of these genes means a woman has an increased risk for developing breast or ovarian cancer but it does not mean cancer is inevitable. Researchers do not yet know the extent to which BRCA-1/BRCA-2 gene mutations affect a woman's risk for cancer, though believe they are responsible for about 5 percent of breast and ovarian cancers. Many factors influence the development of cancer; genetics remains only one among them.

Testing for BRCA-1/BRCA-2 is controversial because there are few preventive or therapeutic actions women or doctors can take as a result of knowing a positive result. Under current practice guidelines, doctors may choose to offer such testing to women who have first-degree relatives (mother, daughter, sister, grandmother) who have breast cancer or ovarian cancer or who are themselves under age 50 at the time of being diagnosed with either type of cancer. A positive result (mutations are present) may be a factor in prophylaxis or treatment decisions, though is by itself not a strong enough indicator to be the basis for such decisions. Nor is a negative result any indication that a woman will not develop breast or ovarian cancer. Because doctors can detect breast and ovarian cancers early through regular examinations, most health experts believe such examinations remain the most effective means for early diagnosis and treatment regardless of genetic influences.

See also CA-125; GENETIC TESTING; MUTATION; PROSTATE-SPECIFIC ANTIGEN (PSA).

C

cancer risk factors The circumstances that may increase an individual's chance for developing cancer. Cancer risk is a combination of hereditary, environmental, viral, bacterial, immunologic, and lifestyle factors that alter CELL STRUCTURE AND FUNCTION. Age is the most significant single risk factor for cancer, with most cancer developing in people age 50 and older. This reflects current thinking that most cancer results from cumulative damage to cellular DNA, which causes changes in cells as they divide.

Gender is a significant risk factor for specific cancers. For example, BLADDER CANCER is three times more common in men than women, and only about 1 percent of BREAST CANCER occurs in men. Ovarian and endometrial cancers are uniquely women's cancers, and TESTICULAR CANCER and PROSTATE CANCER are uniquely men's cancers. LIVER CANCER and PANCREATIC CANCER are also more common in men. Hereditary genetic factors influence the risk for breast cancer, ovarian cancer, and COLORECTAL CANCER.

The most significant mutable (changeable) risk factor for cancer is cigarette smoking, which accounts for 85 percent of LUNG CANCER, 60 percent of bladder cancer, and about 30 percent of other cancers collectively. Excessive ALCOHOL consumption and exposure to environmental carcinogens (substances that cause cancer) are also preventable risks for cancer.

Infectious agents are emerging as major risk factors for certain cancers. Researchers have already linked certain cancers with specific infections. More than 90 percent of women who have CERVICAL CANCER also have HUMAN PAPILLOMAVIRUS (HPV) INFECTION. About 80 percent of people who have STOMACH CANCER test positive for the presence of *HELICOBACTER PYLORI*, which causes a low-grade bacterial infection in the stomach. In Western cultures, KAPOSI'S SARCOMA occurs nearly exclusively in people who have HIV/AIDS.

See also BACTERIA; BRCA-1/BRCA-2; CANCER PREVENTION; COLONOSCOPY; MAMMOGRAM; PARASITE; PROSTATE-SPECIFIC ANTIGEN (PSA); SMOKING AND HEALTH; VIRUS.

cancer treatment options and decisions The methods and protocols available to treat cancer and its symptoms. Most cancer treatment involves a combination of methods. There are a number of conventional treatment options for cancer:

- SURGERY FOR CANCER, in which the doctor performs an OPERATION to remove the cancer, is the treatment of first choice for most solid tumors (cancer that develops in organs and tissues other than the BLOOD, LYMPH, or BONE MARROW). The surgery generally removes the tumor and a safe margin of healthy tissue surrounding the tumor in the attempt to prevent stray cells at the tumor's periphery from migrating into other tissues. Sometimes the operation to remove the cancer involves removing an entire structure or organ to obtain such a margin.
- RADIATION THERAPY may precede or follow surgery or may be the sole or an adjuvant treatment. Radiation therapy targets high-energy particles at the cancer cells. The energy—radiation—disrupts the ability of the cancer cells to grow and divide. The cells die, and the body's natural mechanisms (such as PHAGOCYTOSIS) eliminate their debris. Radiation before surgery shrinks the tumor. The main purpose of radiation therapy after surgery is to kill any lingering or stray cancer cells. The oncologist may also combine radiation therapy with CHEMOTHERAPY

CANCER RISK FACTORS

Risk Factor	Type of Cancer
age 50 years and older	all cancers
ALCOHOL consumption	STOMACH CANCER, LIVER CANCER, PANCREATIC CANCER
cigarette smoking	cancers of the lung, BLADDER, kidney, STOMACH, BREAST, prostate, COLON, PANCREAS; acute myeloid LEUKEMIA (AML)
EPSTEIN-BARR VIRUS	Burkitt's lymphoma
gender: female	BREAST CANCER, ENDOMETRIAL CANCER, CERVICAL CANCER
gender: male	BLADDER CANCER, PROSTATE CANCER, pancreatic cancer, stomach cancer, CANCER OF THE PENIS, TESTICULAR CANCER, liver cancer
HELICOBACTER PYLORI INFECTION	stomach cancer, gastric lymphoma
HEPATITIS B VIRUS/hepatitis C virus	liver cancer
HIV/AIDS	KAPOSI'S SARCOMA, lymphoma
human herpes virus-8 (HHV-8)	Kaposi's sarcoma
HUMAN PAPILLOMAVIRUS (HPV) infection	cervical cancer, cancer of the PENIS, vaginal cancer, anal cancer, cancer of the VULVA
human T-lymphotropic virus-1 (HTLV-1)	adult T-cell leukemia/lymphoma (ATL)
INFLAMMATORY BOWEL DISEASE (IBD)	COLORECTAL CANCER
INTESTINAL POLYP	colorectal cancer
personal or family history of cancer	all, though notably breast, ovarian, and colorectal cancers
Schistosoma haematobium parasitic infection	bladder cancer
sun exposure	SKIN CANCER: basal cell CARCINOMA, squamous cell carcinoma, malignant melanoma
TOBACCO USE OTHER THAN SMOKING	oral cancer (lips, tongue, other structures of the MOUTH)

or IMMUNOTHERAPY for an additive effect. Adverse side effects generally stay localized (remain in the area exposed to the radiation).

- Chemotherapy uses drugs to kill cancer cells. Like radiation therapy, chemotherapy may precede or follow surgery to shrink tumors or kill residual cancer cells, serve as the sole treatment, or function as an adjuvant treatment in combination with other treatment methods for optimal effectiveness against certain types of cancer. Because chemotherapy affects the entire body, it can have significant side effects.
- Immunotherapy, also called biological response modification, uses methods to enhance the ability of the body's natural IMMUNE SYSTEM functions to target cancer cells for containment and destruction. Genetically engineered substances such as MONOCLONAL ANTIBODIES (MABS), INTERFERONS, and INTERLEUKINS are among the immunotherapy agents oncologists may administer to boost the IMMUNE RESPONSE.
- HORMONE THERAPY targets HORMONE-driven cancers such as PROSTATE CANCER, OVARIAN CANCER, ENDOMETRIAL CANCER, and BREAST CANCER. These cancers require hormones, typically ESTROGENS or TESTOSTERONE, to grow. Treatment either suppresses or boosts the presence of these hormones in the body. HORMONE THERAPY for breast cancer, for example, deprives the woman's body of estrogen or the ability to use it, and hormone therapy for prostate cancer deprives the man's body of testosterone or the ability to use it. Hormone therapy for prostate cancer may also include administration of estrogen in a further effort to shut down the tumor's hormone sources.
- BONE MARROW TRANSPLANTATION is a treatment option for LEUKEMIA, MULTIPLE MYELOMA, and lymphoma. BONE marrow transplantation replaces cancerous bone marrow with healthy marrow from a genetically matched donor called an allogeneic transplants (a syngeneic transplant when the donor is an identical twin). An autologous transplant uses the patient's own bone marrow, which is an option only when the cancer is in remission or when it does not involve the bone marrow. Bone marrow transplantation may sometimes be a treatment option for other types of cancer though has not proven to be as effective as originally hoped.
- Stem cell transplantation may be a treatment option in cancers that do not involve the bone marrow. The person's stem cells (precursors for red blood cells, white blood cells, and platelets) are gathered from the person's blood, then reinfused into the person after CHEMOTHERAPY.

Though there are established approaches, called treatment protocols, for most types of cancer, cancer treatment is highly individualized and treatment decisions evolve as a collaboration between the person who has cancer and the health-care team providing care for the person. The treatment decision process begins with consideration of the cancer's type, stage, and grade—the characteristics of the cancer cells, how widespread within the body the cancer is, and how aggressive the cancer cells are in their growth pattern. Other important factors include the person's age and overall health status, any other health conditions, and the person's preferences or goals for treatment.

INFORMATION MANAGEMENT

Because there is so much information to absorb and sort through when it comes to CANCER TREATMENT OPTIONS AND DECISIONS, it is a good idea to have a trusted family member or friend go along for key doctor visits to take notes. This lets the patient focus on the discussion with the doctor during the visit with the opportunity to later go over the notes and consider the options.

Sometimes there are clear "best" choices for treatment. Other times there are several treatment options that are likely to produce similar results. A person whose cancer is widespread (metastatic) by the time of diagnosis may choose only palliative treatment—treatments to relieve PAIN and other symptoms—or may choose to enter a clinical trial, a research study evaluating a new treatment that shows promise for the person's particular type or stage of cancer. Each treatment method has benefits and risks, which are important to consider when evaluating the various options.

A second opinion consultation from another oncologist (cancer specialist) is often helpful when there are numerous treatment options or when

treatment options appear slim. Different oncologists may view the same person's situation differently based on their level of experience and knowledge of specific cancers or treatments. Oncologists who practice through medical centers affiliated with research facilities, such as are common at large universities that have medical schools, often know of the newest drugs and therapies under evaluation in current or upcoming clinical trials.

There is an abundance of information about cancer available on the Internet and in publications; sorting through it all to determine what is reliable and what is potentially useful for an individual is confusing and often overwhelming. Because there are no controls over the content of Web sites in particular, a large amount of information is, unfortunately, inaccurate or potentially harmful; with the emotional factors that surround a cancer diagnosis, it is important to make treatment decisions based on sound principles. Many cancer treatment centers have staff and resources to help people put such information into contexts that are relevant for their personal situations. The American Cancer Society (www.cancer.org) and the US National Institutes of Health's (NIH's) National Cancer Institute (www.cancer.gov) provide numerous resources to help people sort through treatment claims and methods.

See also ALTERNATIVE AND COMPLEMENTARY REMEDIES FOR CANCER; BLOOD STEM CELLS; CANCER PREVENTION; COPING WITH CANCER; DIAGNOSING CANCER; END OF LIFE CONCERNS; QUALITY OF LIFE; STEM CELL; SURGERY BENEFIT AND RISK ASSESSMENT.

cancer vaccines Preventive therapies to keep cancer from developing in people who do not have it or to keep cancer from growing or recurring in people who have it. Most cancer vaccines remain in clinical trials. Two approved by the US Food and Drug Administration (FDA) are those for HEPATITIS B VIRUS (HBV), the virus primarily responsible for LIVER CANCER, and for some types of HUMAN PAPILLOMAVIRUS (HPV), the virus primarily responsible for CERVICAL CANCER. Preventing the viral infection nearly eliminates the risk for developing the cancer.

The HBV vaccine is among the recommended childhood vaccines in the United States, given as a series of three shots in infancy. Adults may also receive the HBV vaccine. Health experts recommend routine HPV vaccination for girls between ages 11 and 12, and for all young women to age 26. The HPV vaccine is a series of three injections given over 6 months. The vaccine protects against infection with HPV types 6 and 11, which cause genital warts, and types 16 and 18, which can cause cervical cancer. Both vaccines are effective indefinitely. However, the HPV vaccine is not effective in women who already have HPV infection.

Therapeutic cancer vaccines target an individual's cancer specifically, using antigens from the cancer cells to stimulate an IMMUNE RESPONSE against those cells. The laboratory makes a vaccine using cancer cells from the person. These cells contain the antigens for which the vaccine will stimulate the IMMUNE SYSTEM to produce antibodies. Therapeutic vaccines showing promise in clinical trials target PROSTATE CANCER, some types of BREAST CANCER, some types of LYMPHOMA, and some types of LUNG CANCER.

See also ANTIBODY; ANTIGEN; CANCER TREATMENT OPTIONS AND DECISIONS.

CA-125 Cancer ANTIGEN 125, a protein often elevated in the BLOOD circulation when certain cancers are growing in the body. The cells of the OVARIES, UTERUS, and FALLOPIAN TUBES produce CA-125; consequently CA-125 levels rise in OVARIAN CANCER, ENDOMETRIAL CANCER (cancer of the uterus), and CERVICAL CANCER. The most pronounced elevation occurs with ovarian cancer. However, numerous factors other than cancer can produce elevated CA-125 levels, including benign OVARIAN CYST and UTERINE FIBROIDS. Though an elevated CA-125 level may be one of numerous diagnostic factors the doctor considers when evaluating the possibility of a cancer diagnosis, this tumor marker by itself is not a reliable indicator of cancer. A blood test measures CA-125.

See also CARCINOEMBRYONIC ANTIGEN (CEA); GENETIC TESTING; ONCOGENES; PROSTATE SPECIFIC ANTIGEN (PSA); TUMOR MARKERS.

carcinoembryonic antigen (CEA) A protein present in the BLOOD circulation with certain types of cancer. In this regard, CEA serves as a tumor

marker. The cancers associated with elevated blood CEA levels are carcinomas of the COLON and RECTUM (COLORECTAL CANCER), PANCREAS, STOMACH, BREAST, and lung. The developing fetus also produces CEA, as do benign (noncancerous) tumors of the gastrointestinal tract. In these circumstances the presence of CEA in the blood circulation is normal and not an indication of cancer. Cigarette SMOKING AND CANCER treatment with CHEMOTHERAPY or RADIATION THERAPY also can produce elevated blood levels of CEA.

See also BREAST CANCER; CA-125; CARCINOMA; LUNG CANCER; PANCREATIC CANCER; STOMACH CANCER; TUMOR MARKERS.

carcinogen A substance that can cause cancer. The most common carcinogen is cigarette smoke, which is implicated in nearly all types of cancer and most specifically LUNG CANCER, BREAST CANCER, PROSTATE CANCER, pharyngeal cancer, STOMACH CANCER, and COLORECTAL CANCER. Other significant carcinogens include

- radon, a naturally occurring gas that results from the deterioration of naturally occurring uranium ubiquitously present in rocks and soil
- radiation, such as from overexposure to sunlight (ultraviolet) or ionizing radiation such as X-RAY and gamma-ray
- industrial chemicals such as benzene, vinyl chloride, and arsenic
- pharmaceutical agents such as hormones (oral contraceptives, estrogen supplements)

Some substances are beneficial in small amounts and carcinogenic in large amounts or in cumulative exposure over time, such as sunlight. Certain medications, notably IMMUNOSUPPRESSIVE MEDICATIONS and estrogen-containing drugs, may cause cancer. Others are hazardous at nearly any exposure level. CHEMOTHERAPY drugs, which effectively treat and cure many types of cancer, are themselves carcinogenic for certain types of LEUKEMIA and LYMPHOMA. RADIATION THERAPY as well increases the risk for subsequent cancers, depending on the site of irradiation. Pathogens such as viruses and BACTERIA cause certain kinds of cancer.

Limiting exposure to carcinogens reduces the likelihood that they will have adverse health effects. In the United States, federal and state regulations provide guidelines for occupational exposure to carcinogens. Other public health measures attempt to reduce carcinogen exposure through educational efforts.

COMMON CARCINOGENS

aflatoxins	arsenic
asbestos	benzene
beryllium	cadmium
chromium	cigarette smoke
cyclosporine	diethylstilbestrol (DES)
EPSTEIN-BARR VIRUS	ESTROGENS
ethylene oxide	formaldehyde
HELICOBACTER PYLORI	HEPATITIS B VIRUS
HUMAN PAPILLOMAVIRUS (HPV)	iodine-131
ionizing radiation	methyl chloride
radon	sunlight
tobacco	vinyl chloride

See also ASBESTOSIS; BERYLLIOSIS; CANCER PREVENTION; CANCER RISK FACTORS; ENVIRONMENTAL CIGARETTE SMOKE; ENVIRONMENTAL HAZARD EXPOSURE; LIFESTYLE AND CANCER; OCCUPATIONAL HEALTH AND SAFETY; PATHOGEN; RADON EXPOSURE; SMOKING AND CANCER.

carcinoma A cancerous tumor that arises from epithelial cells. Epithelial cells form the surface layer of tissue throughout the body: the SKIN, mucous membranes, and serous membranes (lining of the internal body cavities). Carcinoma is the most common form of cancer. A carcinoma generally carries the name of the tissue or site of its origin; for example, basal cell carcinoma originates in the basal cells of the skin and ADENOCARCINOMA originates in a glandular structure. Treatment depends on the nature, location, and size of the carcinoma and may incorporate surgery, CHEMOTHERAPY, RADIATION THERAPY, and IMMUNOTHERAPY.

TYPES OF CARCINOMA

Tumor	Location
ADENOCARCINOMA	glandular tissue
basal cell carcinoma	SKIN
intraductal carcinoma	BREAST
large-cell carcinoma	lung
lobular carcinoma	BREAST
small-cell carcinoma	lung
squamous cell carcinoma	skin, mucous membranes

See also ADENOMA; ADENOMA-TO-CARCINOMA TRANSITION; BLASTOMA; SARCOMA; SKIN CANCER.

chemotherapy Treatment for cancer that uses cytotoxic drugs (drugs that destroy cells) to kill cancer cells. About half of people who have cancer receive chemotherapy. Chemotherapy is commonly the treatment of first choice for LEUKEMIA, lymphoma, MULTIPLE MYELOMA, metastatic cancers, inoperable cancers, and as adjuvant therapy following or accompanying another method, such as surgery, that is the primary treatment. Sometimes chemotherapy is an appropriate choice for palliative treatment that shrinks cancer tumors to relieve symptoms such as PAIN. The goal of chemotherapy may be to eradicate the cancer or to keep the cancer in check to eliminate its symptoms and keep it from spreading.

How Chemotherapy Works to Treat Cancer

Chemotherapy drugs, also called chemotherapeutics or antineoplastic ("against new growth") drugs, work by interfering with cell growth, activity, or division. Many of them directly damage DNA, the cell's GENETIC CODE that directs the cell's processes for growth and replication. Chemotherapy drugs are toxic to all cells in the body. However, they have the most significant action on cells that are rapidly dividing, such as cancer cells. Most chemotherapy drugs have a NARROW THERAPEUTIC INDEX (NTI); there is a fine margin between their helpful and harmful actions. This narrow margin often causes unpleasant but predictable side effects that subside at the end of treatment.

Chemotherapy Agents

More than 600 chemotherapy drugs are currently available to oncologists, who often combine them in dozens of treatment protocols to treat various types of cancer. Chemotherapy drugs may be administered by MOUTH (oral), injection (intravenous, intramuscular, or subcutaneous), local application (topical or via instilled solution such as into the BLADDER), and intrathecal catheter (into the spinal canal).

Alkylating agents The alkylating agents are the oldest type of chemotherapy drugs and derive from nitrogen mustards, the chemical family to which poisonous mustard gas belongs. These chemotherapy drugs interfere with at least four stages of cell division, making them highly effective against many types of cancer. Consequently many chemotherapy protocols include an alkylating agent. Some of the alkylating agents require METABOLISM by CYTOCHROME P450 (CYP450) ENZYMES, a large group of enzymes in the LIVER that metabolize many kinds of drugs, to be effective. Many factors, including genetic encoding and diet, affect the function and efficiency of CYP450 enzymes.

COMMON ALKYLATING AGENTS

busulfan	carmustine
chlorambucil	cyclophosphamide
dacarbazine	iphosphamide
lomustine	mechlorethamine
melphalan	procarbazine
thiotepa	

Antimetabolites The antimetabolites derive from chemical structures similar to vitamins and amino acids (called metabolites) though are useless to cells. The chemical similarity is so close, however, that cells mistake antimetabolites for substances they need to carry out their metabolic processes. However, the antimetabolites cannot complete those metabolic processes, interfering with the ability of cells to synthesize (make) nucleic acid, an essential component of DNA. Without new DNA, cells cannot divide. Though each antimetabolite agent has specific cancers against which it is most effective, as a group the antimetabolites are particularly effective in treating leukemia, lymphoma, COLORECTAL CANCER, BREAST CANCER, BLADDER CANCER, PANCREATIC CANCER, and osteosarcoma. Antimetabolites have numerous side effects, including NAUSEA, HAIR loss, and tubular nephritis (damage to the KIDNEYS). Oncologists may give leucovorin along with the antimetabolite to counter these side effects.

COMMON ANTIMETABOLITES

6-mercaptopurine	6-thioguanine
arabinosylcytosine	capecitabine
cladiribine	cytarabine
dacarbazine	fludarabine
fluorouracil (5-FU)	gemcitabine
methotrexate	

Antibiotic chemotherapy agents The anthracyclines and the related DRUG bleomycin are antibiotics that come from the FUNGUS *Streptomyces verticillus*, which naturally occurs in soils primarily in Japan though also can be cultivated. These chemotherapy drugs work by forming free radicals that disrupt the structure of cellular DNA. They are particularly effective against leukemia, lymphoma, and many types of CARCINOMA, notably breast cancer. Bleomycin is similar to the anthracyclines, derived also from the *S. verticillus* fungus, but a different chemical composition and action in cells. It is most effective in combination with other chemotherapy agents for treating lymphoma and TESTICULAR CANCER. The most significant SIDE EFFECT of the anthracyclines is damage to the HEART, and of bleomycin damage to the LUNGS, as a result of free radical activity.

COMMON ANTIBIOTIC CHEMOTHERAPY AGENTS

bleomycin	dactinomycin
daunorubicin	doxorubicin
epirubicin	idarubicin
mitoxantrone	

Camptothecins, etoposide, and vinca alkaloids The camptothecins block the function of topoisomerase, an enzyme cells need to synthesize DNA. Their original source was the bark of the *Camptotheca acuminata* tree native to China. Etoposide has the same action but comes from the bark of the mandrake tree. Vinca alkaloids derive from the leaves of the *Vinca rosea* plant, a type of periwinkle. The vinca alkaloids disrupt cell division. Like the alkylating agents, the camptothecins, etoposide, and vinca alkaloids are effective in treating a broad spectrum of cancers from leukemia and lymphoma to carcinomas and some sarcomas.

COMMON CAMPTOTHECINS, ETOPOSIDE, AND VINCA ALKALOIDS

etoposide	vincristine
vinblastine	vinorelbine
irinotecan	topotecan

Taxanes The taxanes come from the bark of the *Taxus brevifolia*—the Pacific yew tree. They work as chemotherapy agents by blocking the ability of cells to form the structures necessary to divide. They also appear to enhance a number of immune functions and are particularly effective in treating some types of metastatic breast cancer. Currently there are two taxanes, each of which is often more effective in combination with other chemotherapy agents than alone. As well, each taxane has specific side effects: docetaxel can cause severe EDEMA (fluid retention) and paclitaxel can cause MUSCLE pain. Both drugs can cause NEUROPATHY (dysfunction of the nerves) and severe depletion of neutrophils (NEUTROPENIA), white BLOOD cells (leukocytes) important for fighting INFECTION. Neutropenia raises the risk for infection.

TAXANES

docetaxel
paclitaxel

Platinum compounds Platinum compounds disrupt cellular DNA function as well as the ability of cells to synthesize DNA. These chemotherapy agents are particularly effective in treating LUNG CANCER, testicular cancer, and colorectal cancer. They can cause kidney damage and neuropathy.

PLATINUM COMPOUNDS

carboplatin	cisplatin	oxaliplatin

Risks, Side Effects, and Complications of Chemotherapy

Because chemotherapy is a systemic treatment, it affects all cells in the body. Those most severely affected are those that grow and divide rapidly. Though cancer cells are at the head of that list, some healthy cells in the body also grow and divide rapidly. Among them are the cells of hair follicles (which produce hair), blood, and gastrointestinal tract, accounting for the most significant side effects of chemotherapy: hair loss, ANEMIA, increased susceptibility to infection, nausea, VOMITING, and DIARRHEA. However, the extent to which these side effects occur varies across the spectrum of chemotherapy drugs, and many people receiving chemotherapy do not experience them.

Medications and complementary remedies such as GINGER may help with chemotherapy-related nausea. ACUPUNCTURE also provides relief from nausea and other discomforts. Antinausea medica-

tions in the 5-HT3 receptor antagonist family (dolasetron, granisetron, ondansetron, and palonosetron) are especially effective. The long-term risks of chemotherapy include increased likelihood of developing another cancer, notably lymphoma or leukemia (especially acute myeloid leukemia with alkylating agents). Repeated chemotherapy, such as with chronic cancers or multiple recurrences, damages and may destroy the BONE MARROW.

HAIR LOSS DURING CHEMOTHERAPY

The cells of the HAIR follicles divide rapidly and thus are highly susceptible to the effects of chemotherapy. Because of this, people lose their hair after undergoing chemotherapy. However, because hair follicle cells are healthy and normal in their structure and function, most of them are able to resume growth and division—and hair production—when chemotherapy ends.

See also ANTIBIOTIC MEDICATIONS; CELL STRUCTURE AND FUNCTION; INVESTIGATIONAL DRUGS; LEUKOCYTE; PHARMACODYNAMICS; PHARMACOKINETICS; RADIATION THERAPY; SURGERY FOR CANCER.

coping with cancer Methods for handling the physical, emotional, financial, and other stresses of a cancer diagnosis. The diagnosis of cancer is a life-altering event, no matter the type of cancer and its prognosis. Few other health conditions evoke such intense emotions. Though each individual responds uniquely, cancer evokes in everyone a recognition of vulnerability and mortality. It is important for each individual to be able to express his or her feelings, fears, anger, worries, and hopes. Some people want to talk about their cancer and their feelings, some people deny their diagnosis or its seriousness, and some people retreat to introspection.

The time of treatment is often very intense, with most of the focus in the person's life shifting to the treatment and its myriad details. Many people find themselves suddenly and completely immersed in an existence that revolves around doctors, hospitals, tests, and procedures. There may be concerns about health insurance coverage or payment for doctor bills, hospital services, treatment, and medications. Hospitals have financial counselors and social workers who can help work through details such as preauthorizations, coverage requirements, and private and government programs that subsidize or pay for care for people who lack the resources.

Many people are able to return to full, active lives after cancer treatment, and their outward appearance may seem the same as before the diagnosis. However, coping with cancer is a lifelong process for most people. Even when treatment concludes, residual effects may remain as reminders of the cancer. People who had surgery have visible scars and may have deformities, NERVE damage, BLOOD vessel or circulatory disruptions, LYMPHEDEMA, or alterations such as COLOSTOMY or reconstruction. As well, there often are ongoing health-care needs, such as doctor visits, medications, blood tests, and imaging procedures. Most people worry, no matter how healthy they are or how many years go by after treatment, about the possibility that the cancer could come back.

No one expects a diagnosis of cancer; when it strikes, it completely disrupts the fabric of everyday life. The cancer diagnosis also affects family members, friends, and co-workers. The person who has cancer must decide who, and how much, to tell about the cancer. Often, treatment requires time away from work and the person may not be able to return to full work activities for quite some time. People who have young children at home are likely to need extended help from family and friends during treatment and recovery. Older people who live alone may also need support with transportation, housekeeping, and cooking.

Despite the all-consuming nature of cancer diagnosis and treatment, it is important for the person to remain engaged in activities of life that bring relaxation, comfort, and joy, such as spending time with family and friends, participating in favorite recreations and hobbies, or traveling. Many people find peace and calm in YOGA, MEDITATION, or prayer. Because there are dimensions to having cancer that only other people who have cancer can fully understand, SUPPORT GROUPS provide a way for the person who has cancer to share their feelings and experiences.

See also LIFESTYLE AND HEALTH; QUALITY OF LIFE.

D

diagnosing cancer The procedures and tests that determine whether cancer is present. The diagnostic journey often begins with an unusual finding on a screening procedure, such as a MAMMOGRAM or PROSTATE SPECIFIC ANTIGEN (PSA) BLOOD test, or diagnostic procedure done for another purpose such as an X-RAY or a complete blood count (CBC). Sometimes the person identifies symptoms, such as the presence of a lump or rectal bleeding.

The initial doctor's evaluation includes a thorough ROUTINE MEDICAL EXAMINATION with specific focus on the abnormal findings; comprehensive PERSONAL HEALTH HISTORY; and appropriate diagnostic tests, which may include any combination of blood tests, X-rays, COMPUTED TOMOGRAPHY (CT) SCAN, POSITRON EMISSION TOMOGRAPHY (PET) SCAN, MAGNETIC RESONANCE IMAGING (MRI), ULTRASOUND, and biopsy.

Biopsy provides the definitive diagnosis for cancer, giving the pathologist the opportunity to examine tissue structure and cell composition. Depending on the location, size, and characteristics of a tumor, the doctor may remove a small sample of tissue or remove the entire tumor. Common methods for sampling tumors include

- fine-needle aspiration, in which the doctor inserts a small needle into the tumor to withdraw a sample of fluid and cells
- core-needle biopsy, in which the doctor inserts a larger needle into the tumor to extract a core of solid tissue
- ENDOSCOPY, in which the doctor inserts an endoscope into the body through a natural opening to examine suspicious tissues and remove samples
- incisional biopsy, in which the surgeon removes a portion of the tumor to obtain a representative tissue sample
- excisional biopsy, in which the surgeon removes the entire tumor

The pathologist then determines, from the diagnostic tests, imaging procedures, and biopsy findings, the cancer's stage and grade—assessments of how extensive the presence of the cancer in the body and how aggressive the growth of the cancer cells. Though most cancers fit within the standard parameters of STAGING AND GRADING OF CANCER, some do not. The doctor may then present the circumstances and diagnostic findings to a review panel of physician specialists, often called the "tumor board," for additional input and assessment. All of these evaluations then help guide the CANCER TREATMENT OPTIONS AND DECISIONS.

See also CANCER PREVENTION; COLONOSCOPY; SURGERY BENEFIT AND RISK ASSESSMENT; SURGERY FOR CANCER.

diet and cancer The ways in which foods and NUTRIENTS influence the risk for cancer, cancer development, and the effectiveness of cancer treatment. A number of foods have emerged that appear to contain substances that have cancer-fighting capabilities. Substances found in foods that appear able to help the IMMUNE SYSTEM suppress the development and growth of cancer cells include calcium, folate (folic acid), carotenoids, vitamin C, flavonoids, lignans, lycopenes, catechins, indoles, and SOY isoflavones. Numerous foods provide these substances. Conversely, foods that are high in saturated fat, highly salted foods,

FOODS THAT SUPPLY CANCER-FIGHTING SUBSTANCES

Cancer-Fighting Substance	Cancer-Fighting Actions	Food Sources
calcium	reduces the irritation bile and fatty acids cause in the gastrointestinal tract particular benefit to reduce risk for COLORECTAL CANCER	broccoli, bok choy, kale, milk, yogurt, cheese, salmon, legumes
carotenoids (beta-carotene, lutein, zeaxanthin)	block growth of cancer cells particular benefit to reduce risk for LUNG CANCER and CERVICAL CANCER	carrots, sweet potatoes, yellow squash, apricots, bell peppers, corn, spinach
catechins	neutralize free radicals	GREEN TEA, grapes, wine, chocolate
flavonoids	protect DNA, neutralize free radicals	carrots, citrus fruits, onions, apples, tomatoes, blueberries, broccoli, soybeans and soybean products
folate (folic acid)	essential for DNA synthesis and repair	beets, broccoli, cabbage, legumes, spinach, avocados, turkey, asparagus
indoles	block the actions of carcinogens to cause cells to mutate particular benefit to reduce risk for BREAST CANCER and PROSTATE CANCER	cauliflower, Brussels sprouts, bok choy, cabbage, broccoli
lignans	maintain cell health particular benefit to reduce risk for breast cancer, colorectal cancer, and prostate cancer	flaxseed oil, flaxseeds, whole grains, pumpkin seeds, cranberries, green tea, black tea
lycopenes	particular benefit to reduce risk for prostate cancer	tomatoes, tomato sauce, pink grapefruit, guava, watermelon
soy isoflavones	block tyrosine kinase, an enzyme that promotes cancer cell proliferation particular benefit to reduce risk for HORMONE-DRIVEN CANCERS (breast cancer, prostate cancer, OVARIAN CANCER, and ENDOMETRIAL CANCER)	fresh soybeans, tofu, soy flour, soy-based foods
vitamin C	ANTIOXIDANT that neutralizes free radicals blocks conversion of nitrates blocks cancer cells from dividing and proliferating particular benefit to reduce risk for ESOPHAGEAL CANCER and STOMACH CANCER	citrus fruits, strawberries, red cabbage, bell peppers, kiwi fruit, mangoes

and preserved foods appear to increase the risk for cancer overall and particularly for cancers of the gastrointestinal tract.

The extent to which nutrients can inhibit tumor growth remains an area of intensive study in CANCER PREVENTION research. Though foods and nutrients are not the sole factors that prevent or cause cancer, they clearly play significant roles in immune function.

See also CANCER RISK FACTORS; DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND CANCER; LYCOPENE.

dysplasia Abnormal changes that are occurring in cells. In dysplasia, rapidly dividing cells form tissue that has an anomalous structure. This structure has the potential of transitioning to cancer. Dysplasia is an early stage of development for all cancers but not all dysplasia becomes cancer. Because there is no way to know which direction dysplasia will go, doctors closely monitor and often surgically remove or otherwise treat dysplasia. ROUTINE MEDICAL EXAMINATION or health screening commonly detects dysplasia, which seldom produces symptoms. Frequently identified dysplasias include cervical dysplasia, which affects a woman's CERVIX, and oral dysplasia, which affects the mucous membranes in the MOUTH.

Doctors classify dysplasia according to the extent of disruption within the tissue. The earliest stage of dysplasia is hyperplasia, in which cells are growing more rapidly than normal but the structural integrity of the tissue remains normal. In mild dysplasia, the excessive cell growth produces erratic and abnormal tissue structure. In severe dysplasia, also called cancer in situ, cell growth and tissue structure are significantly abnormal but the irregularity remains confined to a single site. The risk for cancer in situ to evolve into a full cancer is high.

Treatment for dysplasia depends on the severity and location of the dysplasia as well as other health factors—such as smoking, which increases risk for all types of cancer—or a condition such as INFECTION with HUMAN PAPILLOMAVIRUS (HPV), which increases risk for cervical cancer. Mild dysplasia may revert to normal growth; often the doctor will recommend diligent observation with examination every three to six months to monitor cell activity at the site. Electrocautery (burning), cryotherapy (freezing), laser ablation, and surgical excision are among methods for eradicating dysplasia. Dysplasia may recur, depending on its cause, though in most circumstances does not return after treatment.

See also CELL STRUCTURE AND FUNCTION; LASER SURGERY; PAP TEST.

hormone-driven cancers Types of cancer that thrive on or require hormones for their survival. In men, ANDROGENS (notably TESTOSTERONE) sustain PROSTATE CANCER. In women, ESTROGENS and PROGESTERONE feed many types of BREAST CANCER, OVARIAN CANCER, and ENDOMETRIAL CANCER (cancer of the UTERUS).

Hormone-driven cancers arise in cells that are HORMONE dependent. However, researchers do not know whether hormones cause these cancers to develop or simply fuel them after they form. Researchers do know that breast cancer and ovarian cancer occur more often in women who have extended exposure to estrogen, such as with early onset of MENSTRUATION (MENARCHE before age 12) or late MENOPAUSE (after age 55). The use of oral contraceptives (birth control pills) or hormone replacement therapy (HRT) for menopause may also increase a woman's risk for these cancers, though research continues to investigate these connections.

The correlation between hormones and cancer becomes even less distinct with prostate cancer. Researchers know that testosterone fuels the growth of prostate cancer cells once the cancer develops. But the role of testosterone in the development of prostate cancer is unknown. Unlike estrogen and progesterone levels in women, testosterone levels in men are fairly constant though do decline gradually after age 30. Some researchers believe it is lower testosterone levels that allow prostate cells to mutate, becoming cancerous. Other researchers believe the changing balance between estrogen and testosterone in a man's body as he ages plays a contributing role. Hormone-driven cancers in men and women are more likely after age 50.

HORMONE THERAPY as adjuvant therapy is the standard of care for most hormone-driven cancers. Primary treatment may be surgery to remove the tumor, RADIATION THERAPY, or CHEMOTHERAPY, or a mix of any or all of these treatment options. Oncologists use luteinizing hormone–releasing hormone (LHRH) agonists, which suppress the body's production of androgens and estrogens, to treat prostate cancer in men and breast, ovarian, and endometrial cancers in women. Aromatase inhibitors, which block the body's ability to convert androgens to estrogen, and tamoxifen, which binds with estrogen receptors to block estrogen, are among the hormone therapies oncologists use to treat hormone-driven breast cancers in women.

See also CANCER TREATMENT OPTIONS AND DECISIONS; IMMUNOTHERAPY.

hyperplasia Overgrowth of cells. Hyperplasia, also called hypertrophy, may occur for various reasons. Though the overgrowth of tissue may cause symptoms it is not necessarily cancerous. For example, BENIGN PROSTATIC HYPERPLASIA (BPH) is common in men over age 65 and commonly causes symptoms such as difficult URINATION. Endometrial hyperplasia is similarly common in women approaching MENOPAUSE, causing symptoms such as abnormal uterine bleeding. Typically the structure of cells and tissue in hyperplasia is normal; there is simply an overgrowth. The risk is that hyperplasia will progress to abnormal cells and tissue structure, a precancerous condition called DYSPLASIA. Unless it causes symptoms, hyperplasia does not require treatment other than diligent monitoring.

See also CANCER RISK FACTORS; CELL STRUCTURE AND FUNCTION.

lifestyle and cancer Personal factors that may contribute to the prevention or the development of cancer. The most significant lifestyle factors related to cancer are smoking, diet, OBESITY, and exposure to environmental carcinogens.

Smoking and Other Tobacco Use

Cigarette smoking accounts for 87 percent of LUNG CANCER in the United States, making lung cancer one of the most preventable types of cancer. Cigarette smoking also raises the risk for numerous other types of cancer, including oral cancer, laryngeal cancer, ESOPHAGEAL CANCER, STOMACH CANCER, LIVER CANCER, COLORECTAL CANCER, PANCREATIC CANCER, kidney cancer, BLADDER CANCER, PROSTATE CANCER, BREAST CANCER, and CERVICAL CANCER. Cigar smoking increases the risk for oral cancers (cancers of the MOUTH and lips) as well as lung cancer, pharyngeal cancer, and stomach cancer. Other tobacco use, such as chewing tobacco and snuff, is the primary cause of oral cancers. Not using any form of tobacco removes its risk as a cause of cancer.

Diet and Nutrition

Numerous studies indicate a diet high in fruits, vegetables, and whole grains and whole grain products reduces the risk for most cancers overall and specifically for esophageal cancer, stomach cancer, and colorectal cancer. Researchers believe the NUTRIENTS, antioxidants, and fiber are the key substances that lower cancer risk. Nutrients and antioxidants boost the IMMUNE SYSTEM, improving its ability to detect and eliminate abnormal cells early in their development. Fiber helps absorb toxins in the gastrointestinal tract and move them more rapidly through the digestive process.

Conversely, research demonstrates that a diet high in red meat increases the risk for cancer overall and specifically HORMONE-DRIVEN CANCERS and cancers of the gastrointestinal tract. Red meat is the primary dietary source of saturated fats, which the body uses to synthesize (make) steroid hormones (androgens and estrogens). These hormones fuel the growth of some types of cancer cells in breast cancer, OVARIAN CANCER, ENDOMETRIAL CANCER, and prostate cancer. Whether they may also encourage the development of these cancers remains under investigation.

Some research has established a connection between the length of time food remains in the gastrointestinal tract with the risk for colorectal cancer. A diet high in plant-based, high-fiber foods moves through the digestive process more quickly than a diet high in fat. Some studies show a primarily plant-based diet may move through the body in 6 to 8 hours, while a high-fat, low-fiber diet may take as long as 26 hours to make the digestive journey.

Obesity

The risk for numerous cancers rises with OBESITY. The reasons for this are difficult to separate out. Researchers know that regular physical activity and nutritious EATING HABITS support the health of cells throughout the body as well as foster efficient immune function. These factors are generally lacking in obesity. Further, the increase in adipose tissue prevalent in obesity appears to be a contributing factor to hormone-driven cancers such as prostate cancer and breast cancer, the risks for which are higher in people who have obesity than in people who are of healthy weight.

Exposure to Environmental Carcinogens

Researchers have identified more than a thousand chemicals and other substances that have the ability to cause cancer. Some become hazardous only with repeated excessive exposure over time, and some have a fairly immediate consequence. Chemical exposures are common causes of THYROID CANCER, LEUKEMIA, and LYMPHOMA. The ultraviolet rays of sunlight are perhaps the most common long-term environmental CARCINOGEN, responsible for nearly all SKIN CANCER. Radon, which is present in the soil as a byproduct of deteriorating uranium and other radioactive minerals that occur naturally, is the second-leading cause of lung cancer. RADIATION THERAPY as treatment for cancer is also a carcinogen, raising the risk for lymphoma as well as solid tumors.

Lifestyle Modifications to Decrease Cancer Risk

Nutritious eating habits, daily physical exercise, and avoidance of tobacco products are key ways in which people can modify their lifestyles to reduce the risk for cancer as well as other significant health conditions such as CARDIOVASCULAR DISEASE

(CVD) and DIABETES. Health experts recommend that all homes be tested for radon levels, as basements and foundations can trap radon that emerges from the underlying soil. There are ways to release trapped radon so it does not present a cancer risk. ROUTINE MEDICAL EXAMINATION helps detect precancerous conditions and cancer when it is in its early, treatable stages.

See also CANCER PREVENTION; CANCER RISK FACTORS; DIET AND CANCER; HEALTH RISK FACTORS; RADON EXPOSURE; SMOKING AND CANCER; WEIGHT LOSS AND WEIGHT MANAGEMENT.

M–O

metastasis Cancer that spreads beyond its site of its origin. Metastasis may be local (extend outside the original tumor but remain near the original site), regional (remain in the general vicinity of the original site), or distant (in organs or tissues elsewhere in the body from the original site). It may occur as a result of direct invasion of adjacent tissues and organs or when cancer cells enter the LYMPH or BLOOD circulation. A metastasized cancer retains the characteristics of the tumor of origin. For example, PROSTATE CANCER that metastasizes to the BONE is metastatic prostate cancer, not BONE CANCER. The type of cancer is an important factor in determining the most effective treatment. The LUNGS, LIVER, and bone are the most common sites for metastasis. Cancer that comes back after treatment is a RECURRENCE. Metastasis may be evident at the time of diagnosis or may occur after treatment.

See also CANCER TREATMENT OPTIONS AND DECISIONS; REMISSION.

molecularly targeted therapies Treatment approaches for cancer that interfere with specific molecular functions within cancer cells to prevent them from dividing. The most significant benefit of molecularly targeted therapies is that they can selectively alter the function of specific cancer cells without affecting the function of normal cells. They do so primarily by targeting the protein signals cancer cells use that regulate their growth and division. These signals may be ones that promote growth or regulate APOPTOSIS (natural cell death). The drugs that target them may be signal-transduction inhibitors (also called small-molecule drugs), apoptosis-inducing drugs, and MONOCLONAL ANTIBODIES (MABS).

Current molecularly targeted therapies are especially promising for cancers that have a widespread presence in a vital organ or throughout the body, such as small-cell LUNG CANCER (SCLC) and MULTIPLE MYELOMA, which makes them difficult to treat through other approaches. Because molecularly targeted therapies are so new, doctors do not know their risks or long-term consequences or the extent to which they may be effective in treating cancers in general.

DRUGS USED IN MOLECULARLY TARGETED THERAPIES

bortezomib (Velcade)	gefitinib (Iressa)
imatinib mesylate (Gleevec)	oblimersen (Genasense)
rituximab (Rituxan)	trastuzumab (Herceptin)

See also CANCER TREATMENT OPTIONS AND DECISIONS; CELL STRUCTURE AND FUNCTION; CHEMOTHERAPY; IMMUNOTHERAPY; ONCOGENES; TUMOR SUPPRESSOR GENES.

oncogenes Mutated proto-oncognes that abnormally infuence the rate of growth of cells. Researchers believe oncogenes play a role in the development of cancer by altering cellular growth through one or more mechanisms. Oncogenes may accelerate cell division, block APOPTOSIS (planned cell death), or in other ways allow cells to grow beyond the boundaries of the body's normal controls. MOLECULARLY TARGETED THERAPIES and MONOCLONAL ANTIBODIES (MABS) show significant promise for altering oncogenes to reduce their role in the development of cancer.

Proto-oncogenes are the normal genes which contain the genetic code that tells cells which proteins, and how much of them, to produce to direct the cell's own growth. These proteins, called sig-

naling proteins, act as messengers within the cell. When proto-oncogenes mutate, their genetic instructions become garbled. The protein production they regulate changes. The cell may produce too many proteins that instruct it to grow, or not enough proteins that instruct it to stop growing. In either circumstance the cell's growth becomes excessive.

Oncogenes do not alone cause cancer, though researchers remain uncertain about the extent to which they influence the development of cancer. Other genetic and environmental factors come into play, affecting various aspects of cellular growth. Mutations may occur in the genes that regulate DNA repair, for example, allowing damaged cells to replicate. Researchers believe it is the convergence of factors, the emergence of oncogenes among them that permits cancer to develop.

IDENTIFIED ONCOGENES

Gene	Cancer Connection
bcl-2	B-cell lymphoma and numerous other cancers
c-erb	BREAST CANCER
c-myc	small-cell LUNG CANCER (SCLA), Burkitt's lymphoma
HER-2/neu	breast cancer
hTERT	numerous cancers
ras	numerous cancers
src	breast cancer, colon cancer, SCLA, neuroblastoma, rhabdomyosarcoma

See also CELL STRUCTURE AND FUNCTION; TUMOR SUPPRESSOR GENES.

P

pain management in cancer The ability to improve comfort and provide relief from PAIN and related symptoms that cancer and cancer treatment may cause. Many people worry about the potential for their cancer to cause pain. However, the broad spectrum of available ANALGESIC MEDICATIONS and other methods provide numerous options to manage, and often entirely relieve, pain due to cancer.

Causes of Pain in Cancer

Pain in cancer arises from either the cancer or from treatments for the cancer. Cancerous tumors can cause pain when they invade tissues and disrupt the nerves. Sometimes cancer can also invade NERVE tissue, also causing pain. Damage to structures, such as may occur when cancer invades and destroys tissues and organs, causes the cells of those structures to release numerous CYTOKINES (biochemicals that activate various components of the IMMUNE RESPONSE). Among these cytokines are substances that stimulate nociceptors, specialized molecules in peripheral neurons that send pain signals to the CENTRAL NERVOUS SYSTEM. RADIATION THERAPY is often effective for pain relief in such situations, as it can shrink the tumor so it no longer pressures nerves and other structures. Sometimes surgery to remove part of the tumor also provides relief.

SURGERY FOR CANCER is most often the cause of treatment-related pain. Sometimes surgery for cancer is extensive, and the recovery period can be lengthy and challenging. Most people are eager to recuperate and return to their normal activities as quickly as possible. They may feel taking analgesic medications prolongs their recovery or may fear that taking narcotic medications, the strongest pain relievers, will result in ADDICTION. Neither is true. It may be necessary to take analgesic medications regularly and for an extended time after major cancer surgery to effectively manage the pain. This is important because adequate pain relief not only provides comfort but also allows the body to heal. Protracted pain is emotionally and physically stressful in ways that interfere with HEALING and QUALITY OF LIFE.

Analgesic Medications for Pain Relief

Over-the-counter analgesic medications such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and acetaminophen often provide relief from mild to moderate discomfort and pain. Prescription NSAIDs and narcotic medications may be necessary for moderate to significant pain. Dependence and addiction are very seldom concerns in people who are taking narcotic pain relievers for such levels of pain. As well, there is little risk for overdose, another major concern.

Though there is a ceiling effect with NSAIDs (a point beyond which increasing the dose does not provide any greater pain relief), this is not the case with opioid analgesics. The body seems able to accommodate the effects narcotics have on the respiratory cycle when the narcotics are necessary to relieve high levels of pain. However, opioid pain relievers do impair judgment and thought processes enough to make activities such as driving hazardous and ill-advised.

Palliative Treatments for Pain Relief

Radiation therapy and surgery are often options for palliative treatment for pain resulting from cancer. These treatments reduce the size of tumors, relieving their pressure on surrounding tissues. The relief may extend months to years, depending on the cancer. There is no discomfort

associated with palliative radiation therapy. Palliative surgery does entail recovery from the surgery, though this typically follows a predictable and fairly rapid course after which relief from the cancer pain is often pronounced or complete.

Other Methods of Pain Management

Other methods that may help a person cope with pain include ACUPUNCTURE, BIOFEEDBACK, HYPNOSIS, YOGA, and MEDITATION. These methods incorporate MIND–BODY INTERACTIONS that provide physical, mental, and emotional changes to lessen the effects of pain. Acupuncture is also effective for relieving NAUSEA and other discomforts associated with CHEMOTHERAPY. These methods may be alternatives to medication that allow management of pain and return to normal activities.

See also CHRONIC PAIN; NEURON; TERMINAL PAIN.

R

radiation therapy The use of ionizing electromagnetic energy particles or waves to destroy cancer cells. Radiation is the emission of energy in a pattern of rays, such as visible light. Ionizing radiation is a form of energy of sufficient intensity to alter the electronic charge of atoms and the structure of molecules, such as ultraviolet light. At high exposure, such alteration changes the structures of cells. The effects of ionizing radiation on cellular structure can cause as well as treat cancer.

The substances that contain the ionizing energy particles are radioactive isotopes, also called radionuclides or radioisotopes, most of which occur in the natural environment though scientists can cultivate them in the laboratory for consistency and ready availability. As the radioisotope disintegrates it releases radiation at a known rate, which allows the radiation oncologist to determine the appropriate exposure times and frequencies.

RADIOISOTOPES USED IN RADIATION THERAPY

cesium-137 (^{137}Cs)	cobalt-60 (^{60}Co)
gold-198 (^{198}Au)	iodine-125 (^{125}I)
iodine-131 (^{131}I)	iridium-192 (^{192}Ir)
palladium-103 (^{103}Pd)	phosphorus-32 (^{32}P)
radium-226 (^{226}Ra)	yttrium-90 (^{90}Y)

The radiation oncologist determines which radioisotope or type of radiation to use based on the type of cancer, its location in the body, and how extensively the tumor has spread. Some types of radiation are more effective for penetration to tumors deep within the body and others are more effective for treating tumors close beneath the surface of the SKIN. How rapidly the radioisotope dissipates is important for internal radiation therapy in which the radiation oncologist implants radioactive pellets into the body to directly expose the cancer tumor to the radiation.

How Radiation Therapy Works to Treat Cancer

A key characteristic of cancer cells is that they divide rapidly and without much organization. Radiation therapy works by damaging the DNA within the cells, which prevents them from dividing. Though all cells in the body are vulnerable to such damage, radiation therapy selectively targets the tumor, limiting the exposure of healthy cells to the radiation. Because normal cells do not divide as rapidly as cancer cells and they divide in an organized process, they are able to recover from the radiation exposure. The exceptions are the cells of fast-growing tissues such as skin and HAIR, which may experience some damage as a result of radiation therapy. The radiation oncologist structures shields and blocks to protect healthy tissue from the radiation as much as possible.

A fundamental premise of radiation therapy is fractionation—dividing a lethal DOSE of radiation into numerous sublethal doses administered over a period time. The standard protocol for radiation therapy in the United States delivers the fractionated dosage of radiation daily five days a week for two to nine weeks. Depending on the cancer and the capabilities of the treatment facility, some radiation therapy protocols use radioisotopes and delivery methods that allow fewer doses administered over a shorter time and that vary the intensity of radiation according to the type and location of the cancer.

Types of Radiation Therapy

There are two basic types of radiation therapy, external beam and internal radiation. Some people receive both external beam and internal radiation therapy, depending on the type and location

of their cancer. In external beam radiation therapy, the source of radiation is outside the body, directed toward the tumor using a machine. The radiation oncologist determines the precise point at which the radiation needs to enter the body, called the treatment portal, and places small tattoo dots to mark its boundaries. These tattoos are permanent and serve as the template for aligning the radiation delivery path.

The machine that delivers the radiation therapy is either a linear accelerator (which is most common) or a cobalt machine. These are similar in appearance to a large X-RAY machine. When receiving radiation therapy the person lies on a table beneath the machine, often positioned with supports and blocks to maintain the proper alignment for the radiation to hit the tumor. Each treatment session may take 15 to 30 minutes, though the actual delivery of radiation takes only a few minutes.

Radiation therapy does not hurt or cause any discomfort, though the experience can be somewhat stressful for people who are claustrophobic (become uncomfortable in closed spaces) because the machine is very large and often very close during treatment. Because the source of the radiation is outside the body, the person receives only the directed energy and does not become radioactive. External radiation therapy is often among the treatments for LUNG CANCER, BREAST CANCER, PROSTATE CANCER, COLORECTAL CANCER, Hodgkin's lymphoma, THYROID CANCER, pharyngeal cancer, and some types of brain cancer.

INTRAOPERATIVE RADIATION THERAPY

Another form of external beam radiation therapy is intraoperative radiation, in which the person receives radiation to the surgical bed (site where the surgeon removed the tumor). Intraoperative radiation takes advantage of direct exposure to the site of the cancer to destroy any cancer cells that may have penetrated the tissue surrounding the tumor.

Internal radiation therapy, also called radiation seeding or brachytherapy, more directly targets the tumor with radioactive pellets (radioisotopes encased in thin wire containers) about the size of grains of rice, implanted in the body into or very near the tumor. Internal radiation therapy delivers a higher dose of radiation more directly to the tumor site, and often for a shorter duration, than would be possible with external beam radiation therapy. Internal radiation may be among the treatments for breast cancer, ENDOMETRIAL CANCER, thyroid cancer, CERVICAL CANCER, prostate cancer, and some cancers of the head and neck.

Internal radiation therapy may be

- interstitial, in which the radiation oncologist implants the radioactive pellets into the tumor or the tissue surrounding the tumor
- intracavitary, in which the radiation oncologist inserts the radioactive pellets into a natural body cavity such as the UTERUS or RECTUM
- intraluminal, in which the radiation oncologist inserts the radioactive pellets into a natural body passage such as the ESOPHAGUS or VAGINA

The implantation generally takes place with the person under general, regional, or local ANESTHESIA. After implantation the person is radioactive—that is, he or she emits ionizing radiation that can expose other people to its effects. Sometimes it is necessary to restrict contact with other people until the end of the course of treatment when the radioisotope dissipates enough to emit a level of ionizing radiation that is within safe limits. Sometimes the surgeon implants the pellets after an OPERATION to remove the tumor. An internal radiation implant remains in place for a few days to several weeks in most circumstances, though may remain for a few minutes to a few hours when the dose of radiation is very high and indefinitely when the optimal therapy is low-dose radiation over an extended time.

Risks, Side Effects, and Complications of Radiation Therapy

About half of people who have cancer receive radiation therapy during the course of their treatment. The general short-term side effects of radiation therapy include

- damage to the skin in the treatment area, similar to SUNBURN
- damage to hair follicles in the treatment area, resulting in local thinning or loss of hair

- mild NAUSEA
- tiredness and fatigue

Short-term side effects generally go away after the course of radiation therapy ends. Short-term risks, which are uncommon, include radiation BURNS to the skin and damage to tissues and organs in the treatment area that impairs their function. Long-term risks and complications of radiation therapy include destruction of the BONE MARROW, development of other types of cancer (notably LYMPHOMA and MULTIPLE MYELOMA), and permanent damage to tissues in the treatment area such as skin and MUSCLE. Specific types of radiation therapy have additional risks.

See also CANCER TREATMENT OPTIONS AND DECISIONS; CHEMOTHERAPY; SURGERY FOR CANCER.

recurrence Cancer that returns after treatment. The cancer may come back to its original site or appear in another part of the body. Recurrent cancer that spreads to multiple sites is metastatic. Treatment for recurrent cancer depends on the type of cancer, its location, and the treatment for the original cancer. Recurrent cancer occurs because cancer cells remain in the body after treatment and are able to reestablish themselves. Some cancers recur because their cells are particularly aggressive. Such cancers require increasingly aggressive treatment that may hold the cancer in check for periods of time, though these periods of REMISSION tend to become shorter and the cancer progresses. Other types of cancer persistently recur, such chronic lymphoma. Treatment can effectively manage such cancers for decades.

See also CELL STRUCTURE AND FUNCTION; METASTASIS.

remission The period of time during which a person in treatment for cancer is free from symptoms though the cancer may still be in the body. In complete remission all symptoms disappear; in partial remission some or most symptoms go away. Remission is generally the result, or may be the goal, of RADIATION THERAPY or CHEMOTHERAPY. Remission may last months to years, depending on the type of cancer. Alternating periods of remission and RECURRENCE (return of the cancer and its symptoms) characterize some cancers, such as chronic LYMPHOMA, chronic LEUKEMIA, KAPOSI'S SARCOMA, and SKIN CANCER.

See also METASTASIS.

S

sarcoma Cancer that arises from connective tissue such as BONE, TENDON, CARTILAGE, fat, MUSCLE, and other soft tissues. Sarcomas may also develop within the walls of BLOOD vessels, which contain connective tissue. Treatment generally combines surgery to remove the tumor with RADIATION THERAPY or, less commonly, CHEMOTHERAPY. Radiation exposure, such as occurs with radiation therapy for other cancers or with accidental or industrial exposure, increases the risk for sarcoma.

TYPES OF SARCOMA

Tumor	Location
chondrosarcoma	CARTILAGE
dermatofibrosarcoma	SKIN
fibrosarcoma	fibrous connective tissue (fibroblast proliferation)
hemangiosarcoma	BLOOD vessel
KAPOSI'S SARCOMA	connective tissue of skin, mucous membranes, organs
leiomyoma	smooth MUSCLE, such as the UTERUS
liposarcoma	fatty tissue
neurofibrosarcoma	nerves
osteosarcoma	BONE
synovial sarcoma	synovial membrane of a JOINT

See also ADENOCARCINOMA; BLASTOMA; CARCINOMA; LIPOMA; NEUROFIBROMATOSIS; SURGERY FOR CANCER.

screening for cancer See CANCER PREVENTION.

sentinel lymph node dissection Surgery to remove and biopsy the first LYMPH NODE in the LYMPH network that drains lymph from the location of a cancerous tumor. The sentinel node is important in determining the course of treatment for the cancer because it would be the first lymph structure to which cancer cells would migrate in METASTASIS. During the OPERATION to remove the tumor, the surgeon injects a dye into the tissues at the tumor's location. The first lymph node to show the presence of the dye is the sentinel node, which the surgeon then removes. If cancer cells are in the sentinel node, then the surgeon removes additional lymph nodes and possibly more tissue surrounding the tumor. If there are no cancer cells in the sentinel node, then the surgeon does not need to remove any further tissue. Sentinel lymph node dissection is increasingly common in surgery for BREAST CANCER, malignant melanoma, and other cancers that may remain localized.

See also LYMPHEDEMA; STAGING AND GRADING OF CANCER; SURGERY FOR CANCER.

signs and symptoms of cancer Though each type of cancer has specific signs and symptoms, some symptoms are universal to nearly all types of cancer. Such symptoms include

- unintended weight loss, often rapid
- general sense of not feeling well (malaise)
- fatigue that does not improve with sleep and rest
- unexplained FEVER or night sweats
- swollen though painless LYMPH nodes
- unexplained loss of APPETITE

Early symptoms are general and may indicate numerous health conditions other than cancer. However, early detection and diagnosis of cancer presents the best opportunity for successful treatment. Possible cancer symptoms in combination with risk factors such as age over 50 years, cigarette smoking, or OBESITY are more suspicious.

Specific symptoms of certain cancers that are worthy of a doctor's assessment include

- prolonged COUGH, which may suggest laryngeal cancer or LUNG CANCER
- a wound or sore that does not heal, which may suggest SKIN CANCER
- a change in bowel habits or rectal bleeding, which may suggest COLORECTAL CANCER
- a lump in the BREAST or testicle, which may suggest BREAST CANCER or TESTICULAR CANCER
- extended NAUSEA, VOMITING, or DIARRHEA may suggest ESOPHAGEAL CANCER, STOMACH CANCER, PANCREATIC CANCER, or colorectal cancer

See also BREAST SELF-EXAMINATION; CANCER PREVENTION; DIAGNOSING CANCER; LYMPH NODE; TESTICULAR SELF-EXAMINATION.

smoking and cancer Cigarette smoking is the leading cause of numerous types of cancer. Cigarette smoke contains more than 4,000 chemicals, none of which is beneficial to health and about 60 of which are known carcinogens (cancer-causing substances). Among the key carcinogens in cigarette smoke are formaldehyde, aromatic amines, arsenic, chromium, phenols, tar, and vinyl chloride.

Though LUNG CANCER is currently the leading cause of death from cancer in the United States, health experts believe it is also the most preventable cancer because of smoking's role in its development. Cigarette smoking accounts for 85 percent of the 172,500 people in whom doctors diagnose lung cancer each year. It also accounts for significant percentages of BREAST CANCER, BLADDER CANCER, PROSTATE CANCER, STOMACH CANCER, PANCREATIC CANCER, ENDOMETRIAL CANCER (cancer of the UTERUS), ESOPHAGEAL CANCER, oral cancer (cancer of the MOUTH and lips), laryngeal cancer (cancer of the THROAT), and acute myeloid LEUKEMIA (AML).

Cigarette smoking continues to decline among Americans, with only one in four men and one in five women now being regular smokers. Half of all Americans who ever smoked now no longer smoke. Health experts anticipate a corresponding decline in smoking-related cancers over the coming decades.

See also ANTISMOKING EFFORTS; CANCER PREVENTION; SMOKING AND CARDIOVASCULAR DISEASE (CVD); SMOKING CESSATION; SMOKING AND HEALTH.

staging and grading of cancer The standardized processes and guidelines for assessing the severity of cancer after diagnosis. A cancer's stage and grade help determine the most effective treatment options. Though each type of cancer has its own specific staging and grading protocol, general methodologies apply to nearly all types of cancer, except LEUKEMIA.

Cancer Staging

The stage of a cancer identifies how contained or widespread the cancer is. The traditional method of staging assigns a number to the level of the cancer's severity based on the tumor's location, penetration into lymph nodes, and spread to adjacent or distant tissues. The higher the number, the more extensive the cancer. A stage 0 cancer is small and completely contained, often in situ (confined to the cells in which the cancer started). A stage 4 cancer is widespread with multiple tumors distant from the primary tumor (site where the cancer first started). Staging criteria vary somewhat among the different types of cancer.

GENERAL CANCER STAGING: TRADITIONAL METHOD

Stage	Extent of Cancer
Stage 0	in situ; tumor confined to the cells of its origin
Stage 1	tumor remains localized though has spread beyond the cells of its origin
Stage 2	tumor has spread to adjacent tissues *or* lymph nodes
Stage 3	tumor has spread to adjacent tissues *and* lymph nodes or is locally recurrent
Stage 4	multiple tumors distant from the primary tumor; cancer is recurrent

Another method of tumor staging is the TNM system in which *T* represents the tumor size, *N* represents the involvement of local and regional lymph nodes, and *M* represents METASTASIS to distant sites. The TNM system is internationally standardized and provides more detail about the cancer's characteristics than the traditional, or stage grouping, method. It also allows for more precise characterization of the cancer. As is the

case with traditional staging, criteria vary somewhat among the different types of cancer.

GENERAL CANCER STAGING: TNM METHOD

Stage	Extent of Cancer
Tumor (T)	
T0	no evidence of cancer
Tis	in situ; tumor confined to cells of origin
T1	localized tumor less than 3 centimeters (cm) in size
T2	tumor is larger than 3 cm *or* has invaded adjacent tissues
T3	tumor is larger than 3 cm and has invaded adjacent tissues
T4	large tumor has invaded adjacent tissues or is inoperable
Lymph Nodes (N)	
N0	no cancer in regional lymph nodes
N1	cancer in local lymph nodes
N2	cancer in regional lymph nodes
N3	cancer in lymph nodes beyond the region of the primary tumor
Metastasis (M)	
M0	cancer remains local or regional (no METASTASIS)
M1	cancer has spread to distant sites (metastasis)

Cancer Grading

The grade of a cancer identifies the characteristics of its cells and their growth patterns. Grade is relevant only for cancers that can have varying aggressiveness, such as sarcomas and some types of brain cancer. The pathologist determines the tumor's grade from tissue samples and assigns a numeric value that indicates the tumor's aggressiveness and likelihood for metastasis. As with cancer staging, the criteria differ among the types of cancer, though in general a higher grade value indicates a more extensive or serious cancer. Some tumors have a mix of different cancer cells, in which case the pathologist usually assigns the higher grade to the tumor overall.

Stage, Grade, and Outlook

Oncologists use cancer staging and grading as the general framework for making treatment decisions and assessing prognosis (expected outcome). Though many types of cancer are treatable, controllable, or curable with today's range of treatment options, the individual variation in cancer diagnosis is significant. Each person who has cancer has a unique response based on numerous and sometimes intangible factors. Staging, grading, and other diagnostic parameters represent only a best attempt to characterize a cancer so as to structure an optimal treatment approach; they do not define the outcome.

See also CANCER TREATMENT OPTIONS AND DECISIONS; DIAGNOSING CANCER; LYMPH NODE; TUMOR MARKERS.

surgery for cancer An OPERATION to remove a cancerous tumor. Surgery is the first line of treatment for cancer that a surgeon can readily reach without endangering the person, and when there is a single defined tumor. Multiple tumors may also be appropriate for surgery, depending on the type of cancer, the location of the tumors, and how clearly contained the tumors are. Surgery is typically the primary therapy for treating cancer, with adjuvant (accompanying or follow-up) treatment with RADIATION THERAPY, CHEMOTHERAPY, IMMUNOTHERAPY, or HORMONE THERAPY for a comprehensive approach. A person might undergo chemotherapy or radiation therapy before surgery to shrink the tumor, and also may undergo such treatment after surgery to eradicate any remaining cancer cells.

How Surgery Works to Treat Cancer

Surgery may be therapeutic (attempt to remove the cancer) or palliative (remove enough of the tumor to relieve PAIN or other symptoms). As oncologic surgeons have learned more about how cancer grows and spreads in the body, surgery methods

GENERAL TUMOR GRADING

Grade	Cancer Cell Characteristics	Cancer Aggressiveness
G1	good differentiation, nearly normal cells	low
G2	moderate differentiation, somewhat abnormal cells	intermediate
G3	poor differentiation, abnormal cells	high
G4	no differentiation, unstructured cells	very high

have become more precise. As well, pathology analysis of the tumor has become more efficient and accurate. The surgeon sends samples of the tumor and surrounding tissue to the pathology laboratory during the operation for immediate examination by a pathologist. The pathologist's initial report helps the surgeon determine whether there is a need to remove additional tissue.

In therapeutic surgery the surgeon excises (cuts out) the tumor with a margin of healthy tissue to capture stray cancer cells at the tumor's edges. The goal of such surgery is to eliminate the cancer so the person makes a full recovery and remains cancer free (with or without adjuvant therapies). For large tumors that are difficult to remove, the surgeon may perform cytoreduction (also called tumor debulking) to reduce the size and presence of the cancer as much as possible with the goal of improving the effectiveness of other treatments such as chemotherapy or radiation therapy. In advanced cancer, inoperable tumors may create obstructions or grow into the space an organ ordinarily occupies. The surgeon may perform palliative surgery to remove enough of the tumor to relieve pressure on nerves, BLOOD vessels, and other structures that may be causing pain or interfering with an organ's function.

Types of Surgery

Until the 1990s the standard practice in therapeutic cancer surgery was to remove substantial tissue to ensure removal of the cancer, often resulting in radical surgery such as MASTECTOMY (removal of a BREAST to treat BREAST CANCER) or bowel resection (removal of the COLON to treat COLORECTAL CANCER). Improvements in the understanding of how cancer functions in the body in combination with advances in other treatments for cancer have shifted the approach in cancer surgery toward sparing tissue, organs, and limbs to preserve body structures and functions, relying on a combination of therapies to treat the cancer. When the stage and grade of cancer still requires radical surgery, advances in reconstructive surgery (often performed at the same time as the cancer surgery) have improved QUALITY OF LIFE after surgery.

MINIMALLY INVASIVE SURGERY may be an option for stage 0 cancers, which are small and narrowly confined to the site of origin. OPEN SURGERY is generally the preference for stage 1 and 2 cancers, so the surgeon is able to remove all of the cancer and obtain an acceptable margin of healthy tissue. The length of hospitalization and recovery from the surgery depends on the operation and the person's overall health status. Many people who undergo surgery as primary treatment for cancer are otherwise healthy and typically experience a prompt and uneventful course of recovery.

Risks, Side Effects, and Complications of Surgery to Treat Cancer

Though cancer surgery methods are very advanced, risks and complications are possible. Diagnostic imaging procedures provide the surgeon with a good understanding of where the cancer is and how it involves tissues and organs. However, the surgeon cannot know for certain the nature and extent of the tumor until the surgery exposes it for full examination. Though most surgeries go exactly as anticipated, unexpected findings can shift the operation in a different direction. The surgeon typically recognizes the potential for the unexpected and includes discussion of such possibilities in the informed consent process. It is important to talk with the surgeon the anticipated benefits and potential risks of the planned operation. A second opinion consultation with another surgeon or with a medical oncologist for a discussion of nonsurgical treatment options is often a good idea, particularly when the proposed surgery is extensive or complex.

See also CANCER TREATMENT OPTIONS AND DECISIONS; MOHS'S SURGERY; QUALITY OF LIFE; PLASTIC SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

tumor markers Molecules, often proteins, cancer cells and some other cells produce. Tumor molecules appear in the BLOOD or in the URINE, which makes it possible to measure their concentrations. Elevated levels of certain tumor markers indicate the need for further evaluation to determine whether a cancer is present. However, most tumor markers are not in themselves conclusive for specific types of cancer, even though they may occur in certain cancers as they can occur in numerous benign (noncancerous) conditions. As well, different types of cancer may generate elevations in a particular tumor marker, so elevated concentrations of the marker do not provide information of specific diagnostic value. Oncologists must evaluate tumor marker levels in the context of other clinical findings. Because so many factors influence tumor markers, oncologists disagree as to their usefulness, especially for screening and diagnostic purposes.

Some tumor markers are more useful for monitoring the effectiveness of treatment, because the oncologist can track the fall and rise of the marker's level in the blood circulation. However, tumor markers may rise with successful CHEMOTHERAPY because the dying cancer cells release high quantities of proteins into the blood. After successful treatment, monitoring tumor marker levels may provide early evidence of RECURRENCE should it develop.

COMMON TUMOR MARKERS

Tumor Marker	Corresponding Cancer	Reliability
alpha-fetoprotein (AFP)	LIVER CANCER (hepatocellular cancer); some ovarian cancers; some testicular cancers	moderate for diagnosis
Bence Jones protein	MULTIPLE MYELOMA	effective for diagnosis effective for monitoring treatment
beta-2 microglobulin (B2M)	multiple myeloma; some lymphomas	questionable for diagnosis effective for monitoring treatment
bladder tumor antigen (BTA)	BLADDER CANCER	moderate for diagnosis effective for monitoring treatment
CA-27.29	BREAST CANCER	unreliable for diagnosis in early stages; moderate for diagnosis in metastatic disease effective for RECURRENCE elevation possible in women who do not have cancer

Tumor Marker	Corresponding Cancer	Reliability
CA-72-4	OVARIAN CANCER; STOMACH CANCER; PANCREATIC CANCER; COLORECTAL CANCER	unreliable for diagnosis
CA-125	ovarian cancer	unreliable for diagnosis may be elevated in women who have previously had cancer and are currently cancer free elevated in endometriosis and benign OVARIAN CYST
CA-5-3	breast cancer	unreliable for diagnosis in early stages; moderate for diagnosis in metastatic disease effective for recurrence elevation possible in women who do not have cancer
CA-9-9	pancreatic cancer	moderately reliable for diagnosis
CALCITONIN	medullary THYROID CANCER	effective for diagnosis
CARCINOEMBRYONIC ANTIGEN (CEA)	colorectal cancer; LUNG CANCER; breast cancer	unreliable for diagnosis effective for recurrence elevated in numerous noncancerous health conditions elevated in people who smoke
chromogranin A	neuroendocrine cancers	moderate for diagnosis
HER-2/neu	breast cancer	unreliable for diagnosis moderate for monitoring treatment
human chorionic gonadotropin (hCG)	gestational trophoblastic neoplasia (GTN); TESTICULAR CANCER; ovarian cancer	moderate for diagnosis effective for monitoring treatment
M-protein	multiple myeloma	effective for diagnosis effective for monitoring treatment
NEURON-specific enolase (NSE)	small-cell lung cancer (SCLC)	modest for diagnosis moderate for monitoring treatment
PROSTATE-SPECIFIC ANTIGEN (PSA)	prostate cancer	effective for diagnosis effective for monitoring treatment elevated in BENIGN PROSTATIC HYPERPLASIA (BPH)

See also CANCER PREVENTION; DIAGNOSING CANCER; ONCOGENES; TUMOR SUPPRESSOR GENES.

tumor suppressor genes Genes that stop cell growth, preventing tumor development. In health, tumor suppressor genes direct the production of proteins to block cell division when there are abnormalities in the cell, such as DNA damage. When mutated, tumor suppressor genes lose the ability to influence cell division. Cells may then proliferate without regulation, the foundation of cancer. MOLECULARLY TARGETED THERAPIES and MONOCLONAL ANTIBODIES (MABS) show significant promise for altering the function of mutated tumor suppressor genes to restore their ability to block cell growth.

IDENTIFIED TUMOR SUPPRESSOR GENES

Gene	Cancer Connection
APC	COLORECTAL CANCER
BRCA-1/BRCA-2	BREAST CANCER, OVARIAN CANCER
MEN-1/MEN-2	MULTIPLE ENDOCRINE NEOPLASIA (MEN)
NF1/NF2	NEUROFIBROMATOSIS
PTEN	THYROID CANCER
Rb	RETINOBLASTOMA, osteosarcoma, breast cancer, LUNG CANCER
TP53 (p53)	lung cancer, breast cancer, LIVER CANCER, CERVICAL CANCER, SKIN CANCER, PROSTATE CANCER, ovarian cancer
WT1	WILMS'S TUMOR

See also CELL STRUCTURE AND FUNCTION; GENE; ONCOGENES.

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Dr. Surawicz received her undergraduate degree, a bachelor of arts (B.A.) in biology, from Barnard College in New York City and her medical degrees (M.D.), awarded with honors, from the University of Kentucky College of Medicine in Lexington, Kentucky. She completed her medical internship, medical residency, and gastroenterology fellowship at the University of Washington in Seattle. Dr. Surawicz is board-certified in internal medicine and gastroenterology.

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VOLUME 3

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An Amaranth Book

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To your health!

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The Facts On File Encyclopedia of Health and Medicine in Four Volumes: Volume 3

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VOLUME 3

FOREWORD

A big part of my role as a physician is educating my patients about their health. I take as much time as each person needs to explain prevention measures, test results, and treatment options. I encourage questions. But in the moment, sitting there in my office, most people do not yet know what to ask me. By the time questions flood their thoughts, they may be back at work or at home.

Numerous events and circumstances can challenge health, and we all need to know what actions we can take to keep ourselves healthy as well as to obtain appropriate treatment for health conditions that do affect us. Knowledge empowers all of us to make informed and appropriate decisions about health care. Certainly there is no shortage of reference material. Yet there is *so* much information available today! Even for physicians, it is challenging to keep up. How can you get to the core of what you want to know, reliably and to the level of detail you need?

The Facts On File Encyclopedia of Health and Medicine is a great resource for up-to-date health information presented in a manner that is both comprehensive and easy to understand no matter what your level of medical knowledge. The encyclopedia organizes entries by body system. The progression of body systems—and entries—throughout the encyclopedia presents topics the way you think about them.

Going beyond this basic structure, however, is another layer of organization that particularly appeals to me, which is a comprehensive structure of cross references that integrates entries across body systems. After all, your body functions in an integrated way; so, too, should a reference series that discusses your body's health. Not very much that happens with your health affects one part of your body in isolation from other body structures and functions. Your body attempts to compensate and adjust, often without your awareness, until it can no longer accommodate the injury or illness. The symptoms you bring to your doctor may reflect this compensation, for example frequent headaches that point not to brain tumor (as many people fear but is very rare) but to eye strain or muscle tension or sometimes to hypertension (high blood pressure).

In my medical practice I emphasize integrative health care, embracing the philosophy that health exists as the intricate intertwining of the body's many systems, structures, and functions. So, too, does the care of health. I received my medical degree from Tufts University School of Medicine in Boston, an institution noted for remaining at the forefront of the medical profession. I also completed clinical programs in Mind-Body Medicine at Harvard University, Integrative Medicine at the University of Arizona School of Medicine, and Medical Acupuncture at the University of California-Los Angeles (UCLA). I am a board-certified obstetrician-gynecologist, a board-certified clinical nutritionist, and a licensed acupuncturist. I see patients in my practice in Cincinnati, Ohio; I teach, I lecture, and I frequently go on television and radio to talk about health topics. In each of these areas, I encourage people to think about their health and health concerns from an integrative perspective. When you understand your health from multiple dimensions, you can better understand what to do to keep yourself as healthy as possible.

I wish you the best of health for all of a long, satisfying life. But when the time comes that you must make decisions about medical care, I want you to have the knowledge to make informed

choices that are right for you. Whether you start here and move on to more specialized resources or locate all the information you need within these four volumes, you will find *The Facts On File Encyclopedia of Health and Medicine* to be a most valuable reference resource.

—Maureen M. Pelletier, M.D., C.C.N., F.A.C.O.G.

HOW TO USE
THE FACTS ON FILE ENCYCLOPEDIA OF HEALTH AND MEDICINE

Welcome to *The Facts On File Encyclopedia of Health and Medicine*, a four-volume reference set. This comprehensive resource is an indispensable reference for students, allied health professionals, physicians, caregivers, lay researchers, and people seeking information about health circumstances and conditions for themselves or others. Entries present the latest health concepts and medical knowledge in a clear, concise format. Readers may easily accumulate information and build a complete medical profile on just about any health or medical topic of interest or concern.

A New Paradigm for the Health and Medical Encyclopedia

As the art and science of health and medicine continues to evolve, with complex and elegant discoveries and new techniques, medications, and treatments emerging all the time, the need has arisen for a new paradigm for the encyclopedia of health and medicine—a rethinking of the old, and increasingly outmoded, presentations. Carefully researched and compiled, *The Facts On File Encyclopedia of Health and Medicine* offers many distinguishing features that present readers and researchers with an organization as up-to-date and compelling as the breakthrough information its entries contain.

Recognizing the current emphasis on presenting a truly integrative approach to both health and disease, *The Facts On File Encyclopedia of Health and Medicine* organizes content across volumes within a distinctive format that groups related entries by body system (for example, "The Cardiovascular System") or by general health topic (for example, "Genetics and Molecular Medicine"):

- **Volume 1** presents the sensory and structural body systems that allow the body to engage with its surroundings and the external environment.
- **Volume 2** presents the cell- and fluid-based body systems that transport nutrients, remove molecular wastes, and provide protection from infection.
- **Volume 3** presents the biochemical body systems that support cellular functions.
- **Volume 4** presents topics that apply across body systems (such as "Fitness: Exercise and Health") or that address broad areas within health care (such as "Preventive Medicine").
- The appendixes provide supportive or additional reference information (such as "Appendix X: Immunization and Routine Examination Schedules").

Following Research Pathways

The Facts On File Encyclopedia of Health and Medicine's organization and structure support the reader's and researcher's ease of use. Many encyclopedia users will find all the information they desire within one volume. Others may use several or all four of the encyclopedia's volumes to arrive at a comprehensive, multifaceted, in-depth understanding of related health and medical concepts and information. Researchers efficiently look up information in *The Facts On File Encyclopedia of Health and Medicine* in several ways.

Each section's entries appear in alphabetical order (except the entries in Volume 4's "Emergency and First Aid" section, which are grouped by type of emergency). The researcher finds a desired entry by looking in the relevant volume and section. For example, the entry for **acne** is in Volume 1 in the section "The Integumentary System" and the entry for **stomach** is in Volume 3 in

the section "The Gastrointestinal System." The researcher can also consult the index at the back of the volume to locate the entry, then turn to the appropriate page in the volume.

Terms that appear in SMALL CAPS within the text of an entry are themselves entries elsewhere in *The Facts On File Encyclopedia of Health and Medicine*. Encyclopedia users can look up the entries for those terms as well, for further information of potential interest. Such SMALL CAPS cross references typically provide related content that expands upon the primary topic, sometimes leading the user in new research directions he or she might otherwise not have explored.

For example, the entry **hypertension** is in the section "The Cardiovascular System." The entry presents a comprehensive discussion of the health condition hypertension (high blood pressure), covering symptoms, diagnosis, treatment options, risk factors, and prevention efforts. Among the numerous SMALL CAPS cross references within the hypertension entry are the entries for

- **retinopathy**, an entry in the section "The Eyes" in Volume 1, which discusses damage to the eye that may result from untreated or poorly managed hypertension
- **blood pressure**, an entry in the Volume 2 section "The Cardiovascular System," which discusses the body's mechanisms for maintaining appropriate pressure within the circulatory system
- **stroke** and **heart attack**, entries in Volume 2's "The Cardiovascular System" about significant health conditions that may result from hypertension
- **kidney,** an entry in the section "The Urinary System" in Volume 3, which discusses the kidney's role in regulating the body's electrolyte balances and fluid volume to control blood pressure
- **atherosclerosis, diabetes, hyperlipidemia,** and **obesity**, entries in the sections "The Cardiovascular System" in Volume 2, "The Endocrine System" in Volume 3, and "Lifestyle Variables: Smoking and Obesity" in Volume 4, and all of which are health conditions that contribute to hypertension

Following the path of an encyclopedic entry's internal cross references, as shown above, can illuminate connections between body systems; define and apply medical terminology; reveal a broad matrix of related health conditions, issues, and concerns; and more. The SMALL CAPS cross references indicated within the text of encyclopedic entries lead encyclopedia users on wide-ranging research pathways that branch and blossom.

At the end of the entry for **hypertension** a list of cross references gathered in alphabetical order links together groups of related entries in other sections and volumes, such as **smoking cessation** in Volume 4's "Lifestyle Variables: Smoking and Obesity," to provide specific, highly relevant research strings. These *see also* cross references also appear in SMALL CAPS, identifying them at a glance. Encyclopedia users are encouraged to look here for leads on honing research with precision to a direct pathway of connected entries.

So, extensive cross-references in *The Facts On File Encyclopedia of Health and Medicine* link related topics within and across sections and volumes, in both broad and narrow research pathways. This approach encourages researchers to investigate beyond the conventional level and focus of information, providing logical direction to relevant subjects. Each cross-referenced entry correspondingly has its own set of cross references, ever widening the web of knowledge.

Using the Facts On File Encyclopedia of Health and Medicine

Each section of the encyclopedia begins with an overview that introduces the section and its key concepts, connecting information to present a comprehensive view of the relevant system of the human body or health and medical subject area. For most body systems, this overview begins with a list and drawings of the system's structures and incorporates discussion of historic, current, and future contexts.

Entries present a spectrum of information from lifestyle factors and complementary methods to the most current technologic advances and approaches, as appropriate. Text that is set apart or bold within an entry gives an important health warning, or targets salient points of interest to add layers of meaning and context. Lists and tables

collect concise presentations of related information for easy reference.

Each type of entry (mid-length and longer) incorporates consistent elements, identified by standardized subheadings:

- ***Entries for health conditions and diseases*** begin with a general discussion of the condition and its known or possible causes and then incorporate content under the subheadings "Symptoms and Diagnostic Path," "Treatment Options and Outlook," and "Risk Factors and Preventive Measures."
- ***Entries for surgery operations*** begin with a general discussion of the procedure and then incorporate content under the subheadings "Surgical Procedure," "Risks and Complications," and "Outlook and Lifestyle Modifications."
- ***Entries for medication classifications*** begin with a general discussion of the type of medication and its common uses and then incorporate content under the subheadings "How These Medications Work," "Therapeutic Applications," and "Risks and Side Effects."
- ***Entries for diagnostic procedures*** begin with a general discussion of the test or procedure and then incorporate content under the subheadings "Reasons for Doing This Test," "Preparation, Procedure, and Recovery," and "Risks and Complications."

Entries in Volume 4's section "Emergency and First Aid" are unique within the orientation of *The Facts On File Encyclopedia of Health and Medicine* in that they feature instructional rather than informational content. **These entries do *not* replace appropriate training in emergency response and first aid methods.** Rather, these entries provide brief directives that are appropriate for guiding the actions of a person with little or no first aid training who is first on the scene of an emergency.

Each volume concludes with a complete, full index for the sections and entries within the volume. Volume 4 of *The Facts On File Encyclopedia of Medicine* contains a comprehensive index for all four encyclopedia volumes that researchers can use to quickly and easily determine which volumes contain desired sections or entries.

The Facts On File Encyclopedia of Health and Medicine in Four Volumes

PREFACE TO VOLUME 3

Volume 3 of the four-volume *The Facts On File Encyclopedia of Health and Medicine* presents the body systems that support the body through biochemical functions. From the breakdown of foods into nutrient forms the body can use to the intertwining of hormones with nearly every other body system, biochemistry is the basis of cellular function.

The Gastrointestinal System

Leading Volume 3 is "The Gastrointestinal System," presenting the organs, structures, and functions that deliver nutrients to cells throughout the body. Complex biochemical processes break down all consumed foods into their basic molecular structures, the biochemical forms the body's cells can use.

No matter what a food's original form—apple, steak, french fries—the gastrointestinal system reduces it to molecules. The body then uses the molecules for fuel to maintain cellular activity and metabolism. Among the nutrients essential to sustain life are vitamins, minerals, carbohydrates, proteins, and fats.

As efficient as these processes are for distilling foods into nutrients, there is of course material the body cannot digest or use. The gastrointestinal system takes care of that, too, carrying solid waste from the body.

The Endocrine System

The endocrine system is the body's network of glands and hormones. Glands produce hormones, the chemical messengers that direct myriad activities within the body. The hormones the endocrine system produces interact with every other body system and are responsible for key functions such as metabolic rate, blood pressure, and the sleep-wake (circadian) cycle.

Hormones also manage the processes of digestion. Fat molecules (lipids) are essential for the production of many hormones. Estrogen brings the process full circle through its role in how the body breaks down and uses lipids.

The most common association many people have with hormones is their role to regulate growth and to initiate and maintain secondary sexual characteristics and reproductive ability. Following a person's unique genetic blueprint, hormones determine how fast and how tall the person grows. Hormones also give a man his deep voice and regulate a woman's menstrual cycle.

The Urinary System

The urinary system contains the organs and structures that filter biochemical wastes from the blood and excrete them from the body. All blood passes through the kidneys, which filter from it the wastes of cellular metabolism. If allowed to accumulate in the blood circulation, these wastes rapidly become toxic. Through their filtration functions, the kidneys also maintain the body's fluid and electrolyte levels to help regulate blood pressure. These versatile organs also produce hormones essential for blood pressure regulation.

The kidney was the first organ to be successfully transplanted, and today kidney transplantation is the most commonly performed transplant operation. Thousands of people receive transplanted kidneys every year in the United States; kidney transplantation is the only successful treatment for end stage renal disease, a common complication of diabetes and hypertension (high blood pressure).

Some structures of the male urinary system—the penis, urethra, and prostate gland—do double duty as organs of the male reproductive system.

The Reproductive System

The organs, structures, and functions of the reproductive system make possible the continuation of human life. The reproductive system remains in a state of immaturity until puberty, when the endocrine system initiates hormonal changes to stimulate the development of secondary sexual characteristics. Hormones remain the foundation of reproductive function for all of adulthood.

Pregnancy, the key function associated with the reproductive system, represents an intricate physiologic choreography in which female and male gametes—ovum and sperm—unite to establish a new life. The woman's body carries the new life for nearly 10 months, changing and adapting, as a result of hormones, until it is capable of independent survival.

Psychiatric Disorders and Psychologic Conditions

Biochemical balance and imbalance are integral to the functions and conditions that involve the mind and emotions. The section "Psychiatric Disorders and Psychologic Conditions" brings Volume 3 to a close. Though much of the working of the mind remains a mystery, researchers have made much progress to understand the integrated functions of the endocrine and nervous systems as they relate to psychiatric disorders and psychologic conditions.

Pharmaceutical therapies (medications) to alter neurotransmitter balances in the brain are often the foundation of treatment approaches. Their effects on neurologic function and emotional processes can be profound, even when doctors do not entirely understand the mechanisms of action that produce such results.

THE FACTS ON FILE ENCYCLOPEDIA OF

HEALTH AND MEDICINE

IN FOUR VOLUMES:

VOLUME 3

THE GASTROINTESTINAL SYSTEM

The gastrointestinal system converts ingested foods to nutrients the body can absorb and use. Physician specialists who treat gastrointestinal conditions are gastroenterologists. This section, "The Gastrointestinal System," presents a discussion of gastrointestinal structures and their functions, an overview of gastrointestinal health and disorders, and entries about the health conditions that can affect the gastrointestinal system.

Structures of the Gastrointestinal System

- MOUTH
  - hard palate
  - soft palate
  - cheeks
  - SALIVARY GLANDS
  - TEETH
  - tongue
  - lips
- epiglottis
- ESOPHAGUS
- lower esophageal sphincter
- stomach
  - fundus
  - rugae
  - gastric glands
  - pylorus
  - pyloric sphincter
- LIVER
- GALLBLADDER
- common bile duct
- cystic duct
- hepatic duct
- PANCREAS
- pancreatic duct
- accessory pancreatic duct
- SMALL INTESTINE
  - DUODENUM
  - ampulla of Vater
  - ILEUM
  - JEJUNUM
- COLON
  - APPENDIX
  - CECUM
  - ascending colon
  - transverse colon
  - descending colon
  - sigmoid colon
  - RECTUM
- ANUS

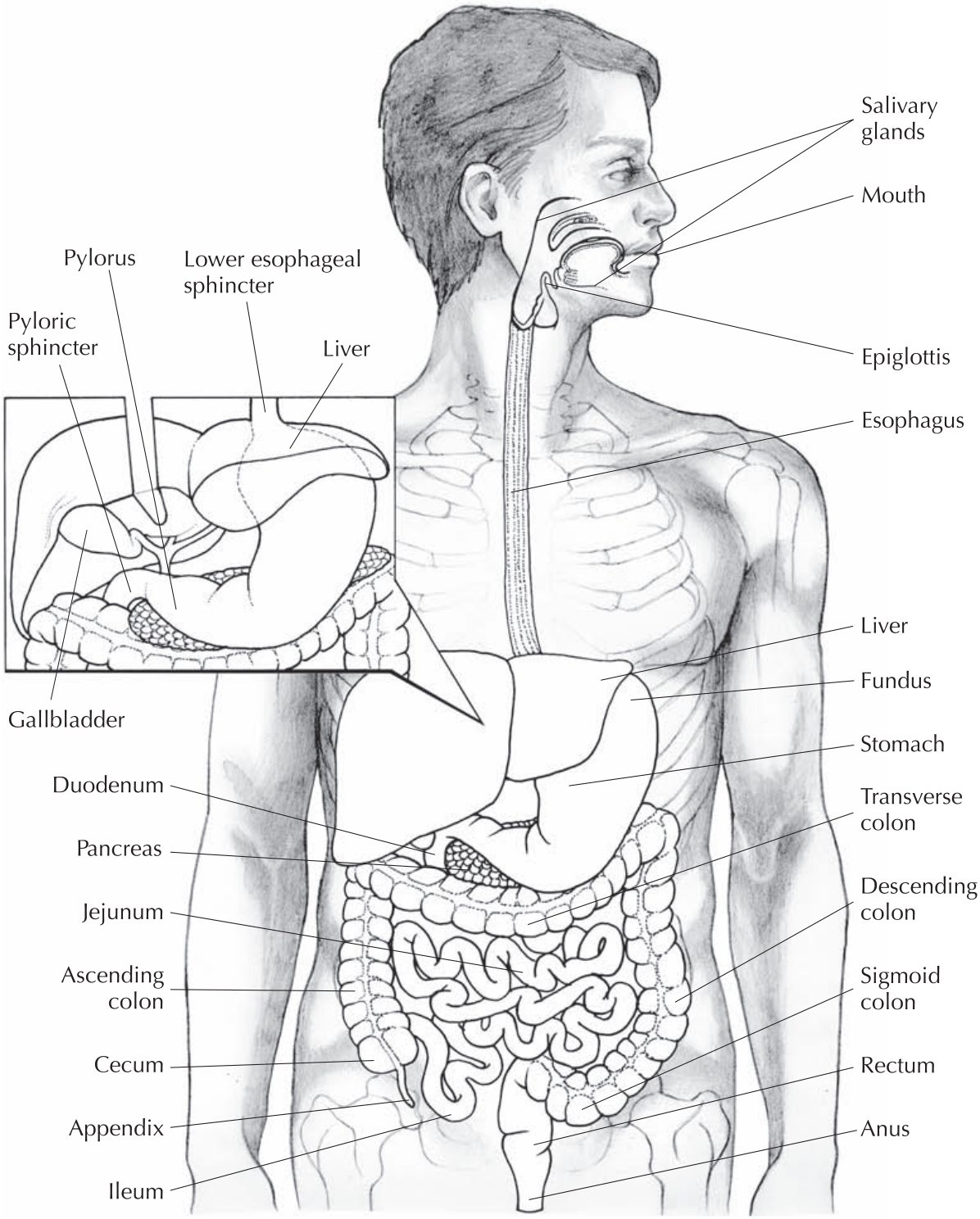
Functions of the Gastrointestinal System

TRADITIONAL CHINESE MEDICINE (TCM), a centuries-old philosophy of health centered on balance among the body's systems and functions, views the torso as the "triple burner" or "triple heater." Here the upper, middle, and lower segments of the body converge, becoming the core that distributes energy throughout the body much like a burner or heater. Western medicine shares a similar understanding, translated into the tangibility of physical structures and their functions.

The gastrointestinal system, also called the digestive or alimentary system, functions as the body's furnace. Fuel—food—enters the gastrointestinal tract in raw form at the MOUTH. Some 20 hours or so later, the compressed residue—feces, also called stool—exits at the other end of the gastrointestinal tract, from the ANUS. Along its passage, the food undergoes numerous transformations as the gastrointestinal organs and structures break it down, mechanically and chemically, into particles and eventually into molecules of energy (NUTRIENTS) that the bloodstream can transport to cells throughout the body. That the typical adult eats three to five times (or more) in 24 hours, yet the body often passes a single BOWEL MOVEMENT in the same period is testament to the gastrointestinal system's efficiency in extracting every molecule, literally, of useful matter from all that food.

The LIVER and PANCREAS produce numerous chemical substances to aid in breaking down the core nutrients of food—carbohydrate, protein, and fat—into molecules that can pass through the membrane of the small intestine to enter the bloodstream. The liver synthesizes BILE, a complex fluid containing water, electrolytes, cholesterol, biliary acids, and BILIRUBIN (400 to 800 milliliters per day). A network of channels, the BILE DUCTS, collect bile from the liver and transport it to the GALLBLADDER. The gallbladder extracts water from the bile to form a concentrated solution, which it stores until DIGESTIVE HORMONES signal the need to release bile for digestion. The bile flows through another duct, the common bile duct, mixes with

The Gastrointestinal System



pancreatic juices, and drains into the DUODENUM, the first part of the SMALL INTESTINE. INSULIN is the best known of the pancreatic products, though the pancreas synthesizes a number of other important hormones, DIGESTIVE ENZYMES, and juices essential for digestion. Digestive hormones orchestrate and synchronize the multitude of gastrointestinal functions.

Mechanical preparation: the mouth The digestive journey begins with the mouth. Each mouthful of food passes between the crushing force of the TEETH, which can exert up to 3,500 pounds per square inch, at least two dozen times. The taste, texture, and smell of the food induce the SALIVARY GLANDS to release saliva, a watery liquid that contains the digestive enzyme amylase. Amylase begins to break down carbohydrates in the food into the sugar molecules that form them, getting a head start on extracting from food the body's most significant fuel source. The lips and cheeks hold the food in the mouth while the tongue pushes the food under the teeth and against the palate (roof of the mouth). These actions grind the food and mix the particles with saliva to form a pastelike wad called a bolus. Finally the tongue pushes the bolus to the back of the THROAT for swallowing. A small projection of cartilaginous tissue that hangs at the back of the throat, the epiglottis, closes across the TRACHEA (windpipe) to direct the bolus of food down the ESOPHAGUS.

Wavelike contractions—PERISTALSIS—propel the bolus down the esophagus, a muscular tube about 12 inches long. The MUSCLE structure of the esophagus changes along its length, transitioning from striated muscle tissue that responds to voluntary control to smooth muscle tissue, completely under direction of the autonomic NERVOUS SYSTEM. Esophageal peristalsis thrusts the swallowed food bolus toward the STOMACH with such vigor that the food continues to its destination even if the person is upside down. A ring of muscle, the lower esophageal sphincter, opens to pass the bolus into the stomach then closes to keep it there.

Liquefication: the stomach The pouchlike stomach can expand to five or six times its empty size to accommodate the meals that come its way. This is where the process of digestion gets under way; the stomach digests more than half the carbohydrates and about 20 percent of the protein that a meal contains. The stomach resides below the DIAPHRAGM, its upper portion resting under the apex of the HEART and near the SPLEEN, just under the left ribs, and its lower portion beneath the liver.

The inside of the stomach is the gastric mucosa, a thick layer of mucous membrane. A network of deep folds, called rugae, gives the gastric mucosa a furrowed appearance. At the bottom of the folds of the rugae are the gastric glands, which produce hydrochloric acid and digestive enzymes (gastric juices). Near the top of the folds are the cells that produce the mucus that protects the stomach's lining from the gastric juices. When the stomach expands with food the rugae flatten, spreading the mucus and expanding the surface area of the stomach for thorough mixing of food with gastric juices. The gastric mucosa also secretes the digestive hormone gastrin.

Three layers of muscle give the stomach STRENGTH and FLEXIBILITY. The innermost layer wraps obliquely, or diagonally, around the gastric mucosa. The middle layer encircles the oblique muscle. The outer layer, the longitudinal muscle, envelopes the stomach lengthwise. Among them, these muscles give the stomach the ability to contract and convolute with considerable force as well as the ability to expand and contract for the volume of food it contains. These layers of muscle also give the stomach the ability to squeeze its contents downward into the small intestine for the rest of the digestive journey.

Food, in a semiliquid state after initial preparation in the mouth, enters at the top of the stomach, called the fundus, and flows downward across the rugae. Gastric juices immediately begin working to dissolve food particles, breaking them down into more basic compounds that the small intestine can digest. At the same time the stomach muscles contract, producing powerful contortions that further mix and liquefy the stomach's contents. The combined chemical and mechanical actions produce chyme, a somewhat soupy solution the stomach then sends to the small intestine. The lower portion of the stomach is the pylorus, from the Greek for "gatekeeper." Chyme exits the stomach through the pyloric sphincter, which relaxes to permit passage into the duodenum. Chyme trickles from the stomach over four to six hours.

Extracting nutrients: the small intestine The small intestine is where nutrients move from the gut to the blood. The nearly 18 feet of small intestine loop back and forth within the abdominal cavity, framed inside the COLON. Two layers of smooth muscle, the outer longitudinal and the inner circular, form the walls of the small intestine. These muscles rhythmically contract to move digestive matter through the gastrointestinal tract. The intestinal mucosa, a thin mucous membrane, forms the inner lining. It produces a number of digestive enzymes and digestive hormones.

In the first segment of the small intestine, the duodenum, the intestinal mucosa is fairly smooth. Only 10 inches long, the duodenum handles the majority of digestive activity. In addition to receiving chyme from the stomach, the duodenum receives bile and pancreatic juices via the common bile duct, which enters the duodenum at a small port called the ampulla of Vater. These solutions complete the breakdown of foods into end-product nutrients. Bile transforms fats into fatty acids. Pancreatic and intestinal enzymes convert proteins to amino acids and polysaccharides (compound sugars) to monosaccharides (simple sugars). Further chemical interactions separate out vitamins and minerals. Monosaccharides and some electrolytes (salts and minerals) enter the bloodstream through the duodenum, which is also the major site for absorption of iron and calcium.

The watery mixture containing the remaining nutrients moves on to the middle and end segments of the small intestine for absorption. In these segments, the JEJUNUM and the ILEUM, millions of tiny projections called villi extend from the intestinal mucosa to vastly expand the mucosal surface area. A network of capillaries (tiny blood vessels) weaves through the villi. Nutrients pass through the mucosal membrane and into the capillaries, which transport them into the bloodstream and throughout the body. The jejunum, about seven feet long, absorbs the remaining monosaccharides and many amino acids, additional electrolytes, water-soluble vitamins (the B vitamins and vitamin C), folic acid, and minerals such as iron. The final segment of the small intestine, the ileum, is about 10 feet long. It absorbs fatty acids and the remaining amino acids, as well as vitamin B_{12} and the fat-soluble vitamins (vitamins A, D, E, and K). The ileum also reabsorbs bile salts. The journey through the small intestine takes 8 to 10 hours.

Compacting waste: the colon The colon, also called the large intestine, collects and compacts the remnants of digestion for their elimination from the body, a process it accomplishes primarily by absorbing water. Like the small intestine, the colon's wall contains two layers of muscle, the outer running lengthwise and the inner circling around, that rhythmically contract. The inner lining is flat mucous membrane. The CECUM, the first segment of the colon, is a pouchlike structure that receives digestive material from the ileum, which enters near its floor. The ileocecal valve maintains the passage for one-way movement. The cecum absorbs about a third of the water from the digestive material it receives. Peristalsis then carries the intestinal content from the cecum through the rest of the colon.

The main colon loops around the outer edge of the abdominal cavity. It contains five segments. The ascending colon rises from the cecum and travels up the body's right side. At the gallbladder the colon takes a turn; the next segment is the transverse colon. The transverse colon extends across the top of the abdomen, with the liver and stomach above and the small intestine beneath. It takes a downward turn at the base of the stomach's fundus, becoming the descending colon. The descending colon drops along the left perimeter of the abdominal cavity. The descending colon makes a staggered turn inward toward the midline of the body, becoming the sigmoid colon. These four segments of the colon are functionally contiguous, progressively dehydrating and compacting the digestive residue that moves through them. The final segment of the colon is the RECTUM, by which point digestive waste has reached the solid form known as feces or stool. The rectum stores stool until its expulsion from the body via the anus (bowel movement). The journey through the colon generally takes four to six hours, though can take longer.

Health and Disorders of the Gastrointestinal System

The gastrointestinal system represents an intricate balance of mechanical and chemical functions.

Lifestyle and dietary habits can affect this balance. To help maintain this balance and preserve gastrointestinal health, gastroenterologists recommend

- Eating foods high in fiber such as fruits, vegetables, and whole grains and whole grain products. High-fiber foods move quickly through the gastrointestinal tract and result in residual bulk that helps keep stools soft, reducing the risk for conditions such as CONSTIPATION and HEMORRHOIDS.
- Reducing consumption of foods high in fats. Fats require more steps to digest, slowing movement through the gastrointestinal tract. Saturated (animal) fats are associated with an increased risk for COLORECTAL CANCER.
- Limiting consumption of products that contain CAFFEINE or ALCOHOL, which are frequent causes of DIARRHEA.
- Drinking plenty of noncaffeinated and nonalcoholic fluids throughout the day.
- Chewing food thoroughly before swallowing and remaining upright after eating.

Gastrointestinal symptoms are the second-leading reason for visits to the doctor, with diarrhea being the most common of these symptoms. Many gastrointestinal ailments are minor, such as INFECTION (GASTRITIS, GASTROENTERITIS, and COLITIS) and irritations such as DYSPEPSIA. The close proximity of the lower esophagus and the bottom of the heart gives rise to the term "heartburn," an apt descriptor for the burning sensation that occurs when gastric contents bubble back up into the esophagus. GASTROESOPHAGEAL REFLUX DISORDER (GERD) develops when such backwash becomes chronic.

Chronic gastrointestinal conditions such as CELIAC DISEASE, DIVERTICULAR DISEASE, IRRITABLE BOWEL SYNDROME (IBS), and INFLAMMATORY BOWEL DISEASE (IBD) can significantly interfere with QUALITY OF LIFE. People who have conditions such as these must work closely with their doctors to develop effective treatment approaches and manage their lifestyles in ways that minimize symptoms and support gastrointestinal health.

Cancers are among the most serious gastrointestinal conditions and can involve any organ or structure of the gastrointestinal system. Though colorectal cancer remains the second-leading cause of deaths due to cancer in the United States, it also offers great opportunity for prevention as well as early detection and treatment. Doctors now know that detecting and removing intestinal polyps, fleshy growths that develop in the colon's mucosa, via screening COLONOSCOPY eliminates the foundation for more than 90 percent of colorectal cancers.

HEALTH CONDITIONS OF THE GASTROINTESTINAL SYSTEM

ACHALASIA
ANAL FISSURE
BARRETT'S ESOPHAGUS
BILIARY ATRESIA
CELIAC DISEASE
COLITIS
CONSTIPATION
CYCLIC VOMITING SYNDROME
ESOPHAGEAL ATRESIA
ESOPHAGEAL SPASM
ESOPHAGITIS
FECAL IMPACTION
FECAL INCONTINENCE
GASTRITIS
GASTROESOPHAGEAL REFLUX DISORDER (GERD)
GASTROPARESIS
HEPATIC ABSCESS
HEPATITIS
HIATAL HERNIA
HIRSCHSPRUNG'S DISEASE
INTESTINAL ADHESIONS
INTESTINAL POLYP
LIVER CANCER
LIVER FAILURE
PANCREATIC CANCER
PEPTIC ULCER DISEASE
PRIMARY BILIARY CIRRHOSIS
PROCTITIS
RAPID GASTRIC EMPTYING
RECTAL PROLAPSE
STEATOHEPATITIS
TOXIC MEGACOLON
WHIPPLE'S DISEASE
ANAL ATRESIA
APPENDICITIS
BEZOAR
BOWEL ATRESIA
CIRRHOSIS
COLORECTAL CANCER
Crohn's disease
DIARRHEA
ESOPHAGEAL CANCER
ESOPHAGEAL VARICES
FAMILIAL ADENOMATOUS POLYPOSIS (FAP)
GALLBLADDER DISEASE
GASTROENTERITIS
GASTROINTESTINAL BLEEDING
HEMORRHOIDS
HEPATIC CYST
HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC)
ILEUS
INFLAMMATORY BOWEL DISEASE (IBD)
INTUSSUSCEPTION
LIVER DISEASE OF ALCOHOLISM
MALABSORPTION
PANCREATITIS
PERITONITIS
PRIMARY SCLEROSING CHOLIANGITIS
RECTAL FISTULA
SHORT BOWEL SYNDROME
STOMACH CANCER
ulcerative colitis
ZOLLINGER-ELLISON SYNDROME

Traditions in Medical History

Ancient doctors learned much about the inner structures and workings of the body from wounds that occurred on the battlefield. The writings of the Roman physician Celsus (14–37 C.E.) documented his recommendations to his students that they take advantage of such natural opportunities. One student who took the advice to heart was GALEN (130–200 C.E.), whose own teachings and writings would shape the understanding and practice of Western medicine for centuries. Galen learned much of the practice of medicine while treating soldiers and gladiators. Of the digestive process, Galen believed stomach liquefied food that then passed to the intestines. From the intestines the mixture traveled to the liver, where it mysteriously became blood that the veins carried around to the various tissues of the body. Though wrong in some fundamental ways, the extrapolation was not so far off from the reality.

In 1822, U.S. Army surgeon William Beaumont became the first physician to witness and explore the functions of the stomach in "real time." In June of that year French-Canadian trader Alexis St. Martin suffered a musket wound to his left side that opened a fist-size hole in his stomach. St. Martin's comrades brought him to Beaumont for treatment. Miraculously in an era of no antibiotics and limited surgical expertise, St. Martin survived. With great scientific curiosity, over several decades Beaumont observed the activities of St. Martin's stomach through this window. He conducted experiments with various items of food tied to string that he periodically withdrew to assess the extent of their demolition in the stomach. He measured the volume and temperature of stomach juices. And he watched the digestive process as much as his schedule and St. Martin's patience permitted.

Finally, in 1833 Beaumont published his findings in a book, *Experiments and Observations on the Gastric Juice and the Physiology of Digestion.* St. Martin lived 58 years with the hole in his stomach, outliving Beaumont by 27 years and dying at age 86. Beaumont's detailed observations and experiments gave modern medicine the most extensive understanding of digestion possible until the 1940s when ANESTHESIA and ANTIBIOTIC MEDICATIONS made surgery practical, and surgeons could more carefully explore the stomach and other gastrointestinal structures.

Breakthrough Research and Treatment Advances

The 21st century arrived on the heels of amazing advances in medical and surgical treatments for gastrointestinal conditions. Among the most significant advances have been those in ORGAN TRANSPLANTATION, which result from a blend of improved surgical techniques, organ harvesting procedures, and immunosuppressive methods. In 1984 LIVER TRANSPLANTATION became the standard treatment for end-stage LIVER FAILURE, a milestone in its progression from experiment to therapeutic solution. Within 15 years surgeons in the United States were performing more than 5,000 liver transplantations a year. Surgeons are now exploring applications for transplantation technology in other conditions, such as to replace the severely diseased small intestine, stomach, and even pancreas. Though these transplant operations remain largely investigational, they hold great promise for people who have disorders such as CYSTIC FIBROSIS, SHORT BOWEL SYNDROME, DIABETES, and severe diverticulosis.

Other advances in diagnostic and operative procedures take advantage of fiberoptic technology. Endoscopic surgery has transformed once-grueling operations, procedures such as open CHOLECYSTECTOMY, which often required up to 12 weeks of recuperation, to a few minor incisions and a third of the recovery time. Surgeons now can perform APPENDECTOMY, herniorrhaphy and hernioplasty, colon resection, and even operations on the stomach with minimally invasive techniques. COLOSTOMY (a surgically created opening through the abdominal wall for the passage of solid digestive waste), once nearly certain after most operations on the colon, now is often temporary or can be avoided altogether. Surgeons have developed methods for anastamosing, or connecting, the remaining segments of the bowel to restore near-normal function. Medications help soothe the bowel and control BACTERIA during HEALING.

The HUMAN GENOME PROJECT, the complete mapping of the human genetic structure, has led to discoveries that have altered the understanding, course of treatment, outlook, and prevention measures for a number of gastrointestinal disor-

ders, including PEPTIC ULCER DISEASE, IBD, and familial cancers of the gastrointestinal tract. GENETIC SCREENING and GENETIC COUNSELING make it possible for people to learn whether they are at risk for many familial or hereditary disorders and take appropriate measures to minimize their likelihood for acquiring the condition. Numerous clinical trials are exploring investigational GENE THERAPY methods to treat or thwart hereditary disorders such as celiac disease and cystic fibrosis.

COLONOSCOPY, visualization of the entire colon using a flexible, lighted endoscope inserted through the anus, has the potential to eliminate 70 percent or more of colorectal cancer through early detection and removal of the adenomatous polyps that are most often the source of cancerous growths in the colon. Research continues the quest for a less intrusive approach, with the current focus on virtual colonoscopy and other procedures that allow for the visualization of the gastrointestinal tract without entering it (though virtual colonoscopy does not offer the opportunity to remove polyps; conventional colonoscopy remains the therapeutic option of choice for most polypectomies). Researchers are also looking for ways to use ENDOSCOPY to screen for other cancers that often go undetected until they are too advanced for treatment, hoping technology may offer similar preventive benefits for a broader range of gastrointestinal malignancies.

A

abdominal distention Swelling of the abdomen, sometimes referred to as bloating. Doctors evaluate abdominal distention as a clinical indicator for a wide range of health conditions. The most common cause of transitory abdominal distention is excessive intestinal gas resulting from eating too fast, which results in swallowing of air along with the food. The BACTERIA in the COLON that ferment high-fiber carbohydrates such as vegetables, fruits, and legumes (beans) also produce intestinal gas during digestion. Infants often swallow air when nursing or bottle feeding, which can cause noticeable abdominal distention rather rapidly. "Burping" the infant relieves the distention. Abdominal distention due to EATING HABITS dissipates as the meal moves through the gastrointestinal system. Completely chewing food before swallowing, especially meats and high-fiber foods, helps slow eating, prepare food for digestion, and reduce the amount of air that enters the gastrointestinal system.

Menstruating women often experience transitory abdominal distention in the few days before and during MENSTRUATION, a result of fluid retention related to hormonal changes taking place in the body. Abdominal distention is a normal feature of PREGNANCY. In early pregnancy the distention and corresponding discomforts may mimic gastrointestinal causes, though as the pregnancy continues the characteristic abdominal enlargement becomes apparent. Extreme OBESITY may mask this presentation, however, resulting in the appearance of generalized abdominal distention rather than characteristic pregnancy. Abdominal distention often is an early sign of ECTOPIC PREGNANCY, a life-threatening condition in which the fertilized egg implants in the fallopian tube instead of the UTERUS. Doctors commonly test for pregnancy in women of childbearing age who seek treatment for abdominal distention.

Abdominal distention that develops gradually and persists may signal health conditions that require medical attention. The most common cause of prolonged abdominal distention is OBESITY, in which excessive body fat accumulates in the central abdomen. The resulting distention may cause the abdominal wall to protrude or cause generalized thickening through the midsection (the "spare tire" presentation of ABDOMINAL ADIPOSITY). Weight reduction results in the gradual recession of abdominal adiposity. ASCITES is a form of abdominal distention that results from fluid accumulating in the peritoneal cavity. Chronic LIVER disease, HEART FAILURE, and chronic KIDNEY disease are among the health conditions associated with ascites. Less commonly, abdominal distention may signal tumors, UTERINE FIBROIDS, OVARIAN CYST, and other growths affecting the abdominal organs. Abdominal distention is a symptom in numerous gastrointestinal conditions including IRRITABLE BOWEL SYNDROME (IBS), MALABSORPTION disorders, and intestinal obstruction.

The doctor should evaluate abdominal distention that persists or in which there is accompanying PAIN, FEVER, or GASTROINTESTINAL BLEEDING. Palpation (feeling the abdomen), BARIUM SWALLOW and BARIUM ENEMA, X-ray endoscopic procedures such as gastroscopy and COLONOSCOPY, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), and paracentesis (withdrawing fluid from the abdominal cavity through the abdominal using a needle and syringe) are among the common diagnostic methods the doctor may use to identify the cause of abdominal distention. Treatment targets the underlying conditions.

See also ABDOMINAL PAIN; BODY SHAPE AND CARDIOVASCULAR DISEASE; DYSPEPSIA; ENDOSCOPY; FALLOPIAN TUBES; FECAL IMPACTION; FLATULENCE; WEIGHT LOSS AND WEIGHT MANAGEMENT.

abdominal pain Discomfort in the trunk region that can range from mild cramping to severe PAIN.

Abdominal pain requires emergency medical attention when:
- **PAIN is sudden, sharp, and unrelenting**
- **Pain radiates into the shoulder or jaw**
- **The abdomen is tense and tender to the touch**
- **There is bloody VOMITING or DIARRHEA**

Abdominal pain is one of the most common reasons people seek medical care. Numerous health conditions can cause abdominal pain, from DYSPEPSIA (indigestion) and FLATULENCE (gas) to APPENDICITIS and GALLBLADDER DISEASE. Advanced or metastatic CANCER, LIVER disease, and HEART ATTACK also can involve abdominal pain, among other symptoms.

COMMON CAUSES OF ABDOMINAL PAIN

APPENDICITIS	cholecystitis
cholelithiasis (gallstones)	CONSTIPATION
dissecting abdominal ANEURYSM	DYSPEPSIA (indigestion)
ECTOPIC PREGNANCY	FECAL IMPACTION
GASTROESOPHAGEAL REFLUX DISORDER (GERD)	HEART ATTACK
	HERNIA
ILEUS (intestinal obstruction)	INTUSSUSCEPTION
NEPHROLITHIASIS (KIDNEY stones)	PANCREATITIS
PELVIC INFLAMMATORY DISEASE (PID)	PERITONITIS
URETHRITIS	URINARY TRACT INFECTION (UTI)
viral GASTROENTERITIS	

It is difficult to gauge the severity of the underlying cause of pain on the basis of the pain's qualities. Intestinal gas can cause immobilizing pain, while heart attack may initially manifest as vague discomfort. FEVER (body temperature above 100° F) often accompanies bacterial infections, which require treatment with ANTIBIOTIC MEDICATIONS. Most abdominal discomfort is transitory and benign. Abdominal discomfort requires medical attention when pain is debilitating or continues for longer than five days without improvement, there is discharge from the PENIS or VAGINA, or there is accompanying VOMITING or DIARRHEA for longer than three days.

See also ABDOMINAL DISTENTION.

achalasia A disorder of the ESOPHAGUS in which the lower esophageal sphincter, the ring of MUSCLE at the entry to the STOMACH, remains constricted, failing to allow food to pass into the stomach. Researchers believe the cause is a reduced number of inhibitory nerve cells, the specialized neurons that direct involuntary muscle tissue to relax. The resulting imbalance allows excitory NERVE cells (neurons that direct involuntary MUSCLE tissue to contract) to dominate. Over time the peristaltic action of the esophagus, a structure of involuntary muscle tissue, slows as well. Symptoms of achalasia include

- painful or difficult swallowing
- regurgitation of swallowed food
- DYSPEPSIA (heartburn)
- PAIN in the central chest and beneath the sternum (breastbone) after eating
- unintended weight loss

BARIUM SWALLOW can suggest the diagnosis, with manometry (which measures the pressure within the esophagus) providing confirmation. The gastroenterologist may also perform esophagogastroduodenoscopy (EGD), an endoscopic examination of the upper gastrointestinal tract, to rule out cancers and to use balloon dilation to gently stretch the sphincter. Some people experience relief with medications, such as calcium channel blockers, which block the actions of excitory neurotransmitters to help relax the lower esophageal sphincter. BOTULINUM THERAPY, in which the gastroenterologist injects botulinum toxin into the sphincter to paralyze it, can provide temporary relief. The treatments of choice for short-term relief are disruption of the lower esophageal sphincter, in which the gastroenterologist uses special instruments to widen the sphincter, or esophagomyomotomy, a surgical OPERATION to cut a portion of the sphincter.

See also ENDOSCOPY; NERVOUS SYSTEM; NEURON; NEUROTRANSMITTER; PERISTALSIS; SWALLOWING DISORDERS.

aging, gastrointestinal changes that occur with The organs and structures of the gastrointestinal system undergo numerous changes as an individual grows older. At birth, the infant's MOUTH supports sucking and swallowing liquid nourishment. With the eruption of TEETH and the elongation of the head, developmental changes that occur in early childhood, the oral cavity shifts to support chewing and swallowing solid foods. By three years of age most children in the United States are eating fully solid foods, their gastrointestinal systems capable of digesting nearly any food an adult's body can accommodate.

The gastrointestinal system remains fairly stable until about the fourth decade of life, at which time changes in muscle tone, vasculature (blood vessel function and blood supply), and body composition begin to affect its structures and functions. Some of these changes are physiologic and others relate to lifestyle; combined they result in increased gastrointestinal problems such as GASTROESOPHAGEAL REFLUX DISORDER (GERD), GALLBLADDER DISEASE, DIABETES (altered functioning of the PANCREAS), and PEPTIC ULCER DISEASE. Changes such as weight gain or OBESITY may affect digestive functions as well, particularly with ABDOMINAL ADIPOSITY, a pattern of body fat distribution in which excess body fat accumulates in the abdomen. This accumulation can compress the intestines, slowing intestinal motility. In the fifth decade of life and beyond, there is increased risk for STOMACH CANCER, LIVER CANCER, PANCREATIC CANCER, and COLORECTAL CANCER.

Changes in vasculature, which often result from other health circumstances such as HYPERTENSION (high BLOOD PRESSURE) and ATHEROSCLEROSIS, affect gastrointestinal motility and absorption. A person age 50 absorbs about a third less calcium than a person age 25. Absorption of other vital nutrients slows as well; many older adults benefit from NUTRITIONAL SUPPLEMENTS. In the seventh decade of life and beyond, the SALIVARY GLANDS and digestive glands slow production of their respective secretions. Reduced saliva makes chewing and swallowing more difficult; reduced gastric juices further impede digestion and absorption. These changes increase the potential for gastrointestinal disturbances such as DIARRHEA and CONSTIPATION.

Measures to preserve gastrointestinal health can mitigate many of the age-related changes that occur in the gastrointestinal system. These include

- eating a high-fiber, low-fat diet
- drinking six to eight ounces of water every hour or two during waking hours
- maintaining healthy weight
- getting daily physical exercise
- having regular screening, such as COLONOSCOPY, for colorectal cancer
- managing other health conditions such as diabetes

See also GENERATIONAL HEALTH-CARE PERSPECTIVES; HYDRATION; MINERALS AND HEALTH; NUTRITIONAL NEEDS; SIALOADENITIS; SIALORRHEA; VITAMINS AND HEALTH.

anal atresia A CONGENITAL ANOMALY, also called imperforate ANUS, in which the anal opening that allows the elimination of feces is missing or misplaced. Diagnosis typically takes place within 24 to 48 hours following birth, with the passage of, or failure to have, the first BOWEL MOVEMENT. Complete anal atresia requires immediate surgery to create a means for the body to pass stool; often the surgeon creates a temporary COLOSTOMY (opening from the large intestine through the abdominal wall) until the infant can undergo any necessary reconstructive surgery. When partial anal atresia is present, the anus may open into another structure such as the VAGINA or URETHRA. Partial anal atresia also requires surgical repair. After surgical reconstruction of the anus many infants have normal bowel function. However some infants have damage to, or are missing, the nerves that regulate the anal sphincter, with resulting FECAL INCONTINENCE. Anal atresia often occurs in combination with other congenital anomalies, notably NEURAL TUBE DEFECTS.

See also BOWEL ATRESIA; CONGENITAL HEART DISEASE; ESOPHAGEAL ATRESIA; RECTAL FISTULA.

anal fissure Small tears in the tissue around the ANUS. Anal fissures can be internal or external. They typically are painful and may bleed with bowel movements, resulting in small amounts of bright red BLOOD on the toilet tissue or in the toilet bowl.

The most common cause of anal fissure is CONSTIPATION, in which the bowel movement is hard and often forced. PAIN can be intense with bowel movements. The doctor can diagnose anal fissure on the basis of the symptoms and by examining the anal area, though may perform an anoscopy to examine the inner anus. Most anal fissures heal with conservative treatment that includes frequent sitz baths, topical application of hydrocortisone preparations to reduce INFLAMMATION, high-fiber diet and stool softeners to pull more moisture into the stools, and daily physical exercise such as walking to improve intestinal motility (movement of food through the gastrointestinal tract) and encourage regular bowel movements.

The next level of treatment for anal fissure that persists is topical nitroglycerin or topical nifedipine (a calcium channel blocker), both of which increase blood flow to the anal sphincter and cause it to relax. Doctors prescribe these medications in oral form to relax the CORONARY ARTERIES as a treatment for CORONARY ARTERY DISEASE (CAD); the pharmacological action on the blood vessels in the anal area is similar. Nitroglycerin ointment, like other forms of nitroglycerin, can cause HEADACHE and dizziness. Another treatment option is BOTULINUM THERAPY, in which the doctor injects the anal sphincter near the fissure with botulinum toxin to temporarily paralyze the MUSCLE fibers, which relaxes the sphincter. The effect of the botulinum toxin lasts about three months. Extensive anal tears and fissures that do not heal with other treatments may require surgical repair. INFECTION may develop with persistent or extensive anal fissure, and requires appropriate antibiotic therapy.

See also ENDOSCOPY; HEMORRHOIDS; PROCTITIS; SITZ BATH.

antacids Products that neutralize gastric (STOMACH) acid to relieve DYSPEPSIA (heartburn and indigestion). Antacids work by increasing the pH (acid level) of the gastric juices, which reduces the irritation to the stomach tissues. Most antacids contain mineral salts, which are alkaline.

Because of their high salt and mineral content, many antacids can cause CONSTIPATION or DIARRHEA by drawing excessive fluid from the gastrointestinal tract. Sodium bicarbonate, which most people mix at home by dissolving baking soda in water, has such a high sodium level that it can affect BLOOD PRESSURE and the rhythm of the HEART. Anyone who has CARDIOVASCULAR DISEASE (CVD), especially HYPERTENSION or ARRHYTHMIA, should not use sodium bicarbonate as an antacid.

COMMON ANTACID PRODUCTS

Active Ingredient	Representative Products
aluminum hydroxide	ALternaGEL
aluminum/magnesium combination	Maalox, Mylanta
bismuth subsalicylate	Pepto-Bismol
calcium carbonate	Tums, Titralac
magnesium hydroxide	milk of magnesia
simethicone	Gas-X, Phazyme
sodium bicarbonate	baking soda

Aluminum hydroxide, though very effective at neutralizing stomach acid, is so likely to cause constipation that it nearly always is combined with magnesium, which has the opposite effect. Doctors may recommend magnesium-based antacids, such as milk of magnesia, as LAXATIVES to treat mild, occasional constipation. Many antacid products also contain simethicone, a surfactant that breaks up intestinal gas bubbles to relieve bloating and FLATULENCE.

Bismuth subsalicylate products such as Pepto-Bismol contain an aspirin-like ingredient that can cause the rare but serious SIDE EFFECT, REYE'S SYNDROME, in children who have viral infections. Children should not take these products.

Antacids are available over the counter, without a doctor's prescription. Occasional use of antacids can provide rapid relief of dyspepsia and other digestive discomforts. Antacids are most effective taken with food, which increases the time the antacid remains in the stomach, and liquid forms seem to be more effective than chewable forms. Chronic or regular use of antacids can result in numerous health problems, ranging from

"rebound" dyspepsia or gastric reflux (most common with calcium carbonate products) to OSTEOPOROSIS (with magnesium products, as magnesium binds with calcium) and aluminum TOXICITY. Indications of antacid overuse include

- dyspepsia symptoms that seem to surge when the antacid DOSE nears the end of its effectiveness
- the need to take higher or more frequent doses of the antacid to obtain relief
- mental CONFUSION (indicating possible aluminum toxicity)
- chronic diarrhea (typically with aluminum/magnesium combination products)

Antacids also interfere with the actions of numerous medications. Other products, such as H2 ANTAGONIST (BLOCKER) MEDICATIONS and PROTON PUMP INHIBITOR MEDICATIONS, are more effective for managing long-term gastric discomfort such as GASTROESOPHAGEAL REFLUX DISORDER (GERD). Antacids also interfere with H2 antagonist blockers. Children age 12 and under should not take antacids unless a doctor recommends them. A pharmacist can suggest an appropriate antacid for the circumstances and to avoid interfering with any medications a person is taking.

See also ANTIDIARRHEAL MEDICATIONS; ANTIEMETIC MEDICATIONS; PEPTIC ULCER DISEASE.

antidiarrheal medications Medications that relieve DIARRHEA. Antidiarrheal medications work by slowing the activity of the gastrointestinal tract or by absorbing more fluid in the COLON (large intestine). Though diarrhea is unpleasant, doctors recommend letting the body restore its balance without medications in most circumstances of acute diarrhea. Acute diarrhea (diarrhea that comes on suddenly) may result from simple gastrointestinal upset following unusual foods and beverages, (such as when traveling), excessive

COMMON ANTIDIARRHEAL MEDICATIONS

Active Ingredient	Representative Products	Availability
attapulgite	Kaopectate, Parepectolin	over the counter
belladonna	Donnatal	requires a doctor's prescription
bismuth subsalicylate	Pepto-Bismol	over the counter
codeine	codeine	requires a doctor's prescription
difenoxin and atropine	Motofen	requires a doctor's prescription
diphenoxylate	Lomotil	requires a doctor's prescription
kaolin and pectin	Kapectolin	over the counter
loperamide	Imodium	over the counter
methylcellulose	Citrucel	over the counter
octreotide	Sandostatin	requires a doctor's prescription
paregoric	camphorated tincture of opium	requires a doctor's prescription
psyllium	Metamucil	over the counter

CAFFEINE consumption, FOOD-BORNE ILLNESSES, or viral INFECTION (GASTROENTERITIS or ENTERITIS). These circumstances tend to resolve themselves within a few days, which may be briefer than the actions of many antidiarrheal medications.

Taking an antidiarrheal product may result in rebound CONSTIPATION. However, diarrhea more significantly interferes with daily activities than does constipation, and many people opt to take medications to slow or stop it. It is important to drink extra fluids when taking antidiarrheal medications, to replace fluids lost with the diarrhea as well as to maintain adequate hydration of the gastrointestinal tract to prevent rebound constipation from developing. Some antidiarrheal medications are available over the counter and others require a doctor's prescription.

Doctors sometimes prescribe anticholinergic medications, which act on the NERVOUS SYSTEM to slow gastrointestinal function, for severe diarrhea. However, these medications have numerous actions throughout the body, and doctors tend to reserve them for use when other antidiarrheal medications are ineffective. Opiate NARCOTICS such as paregoric and codeine are effective for slowing gastrointestinal motility. Attapulgite, pectin, and kaolin are natural substances that absorb fluid. Though typically perceived as LAXATIVES, bulking agents such as psyllium and methylcellulose also absorb water and can help restore normal bowel function.

Antidiarrheal medications are most effective for controlling outbreaks of diarrhea such as may occur with IRRITABLE BOWEL SYNDROME (IBS), INFLAMMATORY BOWEL DISEASE (IBD), and MALABSORPTION. Antidiarrheal medications are also effective for treating antibiotic-induced diarrhea that does not end when the antibiotic therapy ends. Remedies such as taking lactobacillus or eating plain yogurt may help restore normal BACTERIA to the gastrointestinal tract.

The most frequent complication of antidiarrheal medications is rebound constipation. A rare but serious complication that can occur when taking antidiarrheal medications that slow gastrointestinal motility is TOXIC MEGACOLON, in which the colon becomes vastly dilated and flaccid and the flow of the intestinal content stops. Antidiarrheal medications also can mask conditions that require medical attention. For most people, occasional use of over-the-counter antidiarrheal medications provides prompt relief of diarrhea with few complications.

See also ANTACIDS; ANTIEMETIC MEDICATIONS; FIBER AND GASTROINTESTINAL HEALTH.

antiemetic medications Medications that relieve NAUSEA and VOMITING (known clinically as emesis). The most commonly used are anticholinergic medications and antihistamine MEDICATIONS, which suppress the vestibular system mechanisms that cause vomiting. Many antihistamine products are available over the counter. Doctors may recommend or prescribe these medications to treat nausea related to VERTIGO, MÉNIÈRE'S DISEASE, LABYRINTHITIS, and other disorders of the inner EAR and vestibular system, and to help prevent motion sickness. Both anticholinergics and antihistamines can cause drowsiness and dry MOUTH.

A classification of powerful antiemetics, the 5-HT3 RECEPTOR ANTAGONIST MEDICATIONS, became available in the 1990s. Doctors prescribe these medications, such as dolasetron and ondansetron, primarily to treat nausea and vomiting resulting from RADIATION THERAPY, CHEMOTHERAPY, and surgery. These medications work by blocking serotonin from reaching receptors in the gastrointestinal system and may have neurologic side effects such as Parkinson-like symptoms.

Over-the-counter products to treat nausea include bismuth subsalicylate (Pepto-Bismol) and cola syrup, both of which are effective for relieving mild nausea and vomiting with viral INFECTION (such as GASTRITIS and GASTROENTERITIS). Pharmacies also sell a commercial preparation of phosphorated carbohydrate solution, similar to cola syrup, called Emetrol. Cola drinks allowed to go "flat" have the same antinausea effect. These substances act to soothe the inner lining of the stomach. GINGER also has a calming action on the stomach and can provide relief through drinking flat ginger ale (brands that contain ginger, not just ginger flavoring) or eating small pieces of fresh ginger root.

Treatment for nausea and vomiting also targets any underlying conditions or causative circumstances.

See also ACUPUNCTURE; MORNING SICKNESS; NEUROTRANSMITTER.

COMMON ANTIEMETIC MEDICATIONS

Active Ingredient	Representative Products	Availability
bismuth subsalicylate	Pepto-Bismol	over the counter
buclizine	Bucladin-S	requires a doctor's prescription
cyclizine	Marezine	requires a doctor's prescription
dimenhydrinate	Dramamine	over the counter
diphenhydramine	Benadryl	over the counter
dolasetron	Anzemet	requires a doctor's prescription
granisetron	Kytril	requires a doctor's prescription
meclizine	Antivert, Bonine	over the counter (prescription strength also available)
metoclopramide	Reglan	requires a doctor's prescription
ondansetron	Zofran	requires a doctor's prescription
prochlorperazine	Compazine	requires a doctor's prescription
promethazine	Phenergan	requires a doctor's prescription
scopolamine transdermal	Transderm-V	requires a doctor's prescription
trimethobenzamide	Tigan	requires a doctor's prescription

anus The opening through which the body passes solid waste (feces), below the final segment of the COLON and the terminus of the gastrointestinal system. The anal sphincter is a ring of MUSCLE that contracts to contain fecal matter and relaxes to expel it. Learning to control the contraction and relaxation of the anal sphincter begins to take place at age two or three; most children master this control by age four or five. NERVOUS SYSTEM damage, such as with PARKINSON'S DISEASE and sometimes as a consequence of aging, can cause loss of anal sphincter control with resulting FECAL INCONTINENCE.

For further discussion of the anus within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also ANAL ATRESIA; ANAL FISSURE; RECTUM; SPINAL CORD INJURY; STROKE; TRAUMATIC BRAIN INJURY (TBI).

appendectomy A surgical OPERATION to remove an inflamed or infected APPENDIX. The conventional open procedure involves making an incision two to three inches long in the lower right abdomen. Open appendectomy typically requires two or three days of hospitalization and four to six weeks for full recovery. A laparoscopy appendectomy requires a shorter hospital stay and is a more rapid recovery. For a laparoscopic appendectomy, the surgeon makes four or five small incisions (about ½ inch in length). Through one of the incisions the surgeon inserts the laparoscope, a flexible lighted tube. Through the other incisions the

surgeon inserts special instruments. LAPAROSCOPIC SURGERY often requires only an overnight stay in the hospital, with return to normal activities in three to four weeks. Laparoscopic appendectomy is the operation of choice for most circumstances of simple appendicitis in which INFLAMMATION and INFECTION remain confined to the appendix and the diagnosis is clear-cut. The surgeon may choose to convert a laparoscopic to an open procedure should there be any complicating factors once the surgery begins.

Risks of appendectomy, open or laparoscopic, include leakage of intestinal content into the peritoneal cavity, which can result in PERITONITIS, or postoperative ABSCESS (pocket of infection). To safeguard against these complications, postoperative care includes intravenous ANTIBIOTIC MEDICATIONS during the hospital stay and a course of oral antibiotics following hospital discharge. As with any surgery, reaction to ANESTHESIA and bleeding during or after the operation are also risks. Full recovery after appendectomy for simple appendicitis is the norm, with most people returning to their usual activities within six weeks (up to eight weeks for strenuous physical activity such as competitive sports).

See also ENDOSCOPY.

appendicitis INFLAMMATION of the APPENDIX. Because the appendix is so narrow, inflammation can rapidly cause it to swell closed, trapping BACTERIA-laden intestinal matter. This sets the stage for INFECTION that can spread to involve nearby structures.

Appendicitis is an emergency that requires immediate surgery.

The classic symptoms of appendicitis include

- PAIN in the lower right abdomen
- NAUSEA, VOMITING, and aversion to food
- tendency to lie in somewhat of a fetal position, often on the right side with the knees drawn toward the chest

However, more than a third of people who have appendicitis have atypical symptoms that may include diffuse (generalized) abdominal discomfort, pain referred to the back or shoulder area, or symptoms that mimic other health conditions ranging from DYSPEPSIA (indigestion) to URINARY TRACT INFECTION (UTI). Further, there are no definitive causes of appendicitis, though often the surgeon or pathologist detects particles of food or fecal matter lodged in the appendix. The key risk of appendicitis is that the inflamed appendix may perforate (rupture), spilling intestinal debris and infectious matter into the peritoneal cavity. The resulting widespread contamination evolves quickly to PERITONITIS, a life-threatening infection.

The diagnostic path begins with a physical examination to determine the quality of the pain. Key signs of appendicitis during examination include rebound tenderness (increased pain when the doctor presses slowly downward on the abdomen and then suddenly releases the pressure) and pain (often intense) with pressure applied directly over the location of the appendix. A DIGITAL RECTAL EXAMINATION (DRE) also often elicits a significant pain response. A complete blood count (CBC) may reveal the inflammatory process or an infection.

Surgical removal of an inflamed appendix (APPENDECTOMY) provides the only conclusive diagnosis of appendicitis. ANTIBIOTIC MEDICATIONS generally are not effective in treating appendicitis because the infection is generally well under way by the time of diagnosis and the risk of peritonitis or other complicating factors is very high.

See also GALLBLADDER DISEASE; PELVIC INFLAMMATORY DISEASE (PID).

appendix A small, fingerlike projection, sometimes called the vermiform appendix, extending from the bottom of the CECUM, the first segment of the large intestine (COLON). Historically health professionals have viewed the appendix as a vestigial structure with no functional purpose. However, recent research identifies clusters of GUT-ASSOCIATED LYMPHOID TISSUE (GALT), fragments of lymphoid tissue, within the lining of the appendix. Though researchers do not yet understand the role of GALT, they know it belongs to the IMMUNE SYSTEM and has functions related to the IMMUNE RESPONSE. It appears that the immune functions of the appendix, like those of the THYMUS, are most active early in life. Researchers are studying the relation-

ship between the appendix and INFLAMMATORY BOWEL DISEASE (IBD) as well as the role of GALT HYPERPLASIA (enlargement of the lymphoid tissue) in APPENDICITIS. Because of its location and narrow structure, the appendix is vulnerable to circumstances that cause it to become inflamed or infected. Appendicitis is the most common health condition involving the appendix.

For further discussion of the appendix within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also AGING, EFFECTS ON IMMUNE RESPONSE; APPENDECTOMY; MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT).

ascites The accumulation of fluid within the peritoneal cavity. Ascites is an abnormal condition that often accompanies chronic LIVER disease such as CIRRHOSIS and LIVER DISEASE OF ALCOHOLISM. Ascites sometimes also develops with HEART FAILURE, END-STAGE RENAL FAILURE (ESRF), OVARIAN CANCER, and metastatic cancer that infiltrates abdominal structures. Ascites typically causes little discomfort. Paracentesis, in which the doctor uses a needle and syringe to withdraw a sample of the fluid, can help to diagnose the cause of the ascites. The doctor also may use paracentesis to withdraw large amounts of fluid to relieve the ascites. Other treatments include a very low sodium diet and diuretic medications to encourage the kidneys to withdraw larger amounts of fluid from the blood. Untreated or persistent ascites invites PERITONITIS, a potentially life-threatening INFECTION.

See also HEPATITIS; PORTAL HYPERTENSION; STEATOHEPATITIS.

B

barium enema A diagnostic imaging procedure to examine the structures of the lower gastrointestinal tract including the RECTUM and COLON, sometimes called a lower GI (gastrointestinal) series. The gastroenterologist may request a barium ENEMA to help diagnose intestinal polyps, DIVERTICULAR DISEASE, INFLAMMATORY BOWEL DISEASE (IBS), HIRSCHSPRUNG'S DISEASE, intestinal obstruction, COLORECTAL CANCER, and RECTAL PROLAPSE. Preparation for barium enema typically includes a clear liquid diet for two days before the procedure, a laxative the night before the procedure, and an ENEMA the morning before the procedure to cleanse the colon.

The test consists of a barium mixture administered via enema, followed by a series of X-rays (FLUOROSCOPY). Body position and the heaviness of the barium help the barium mixture to flow upward into the lower gastrointestinal tract. For a single-contrast barium enema, the radiologist takes X-ray images of the barium-filled colon and rectum. For a double-contrast barium enema the person eliminates as much barium as possible after the first series of X-rays, then the radiologist injects a small amount of air into the lower bowel and takes another X-ray series. Double-contrast barium enema provides more detailed visualization. The heaviness and pressure of the barium make the procedure uncomfortable and some people experience cramping. The procedure takes 20 to 45 minutes, with the person placed in different positions to help move the barium through the colon. Light-colored stools are normal for several days after the procedure while the barium clears the body. A rare complication is bowel perforation.

See also BARIUM SWALLOW; COLONOSCOPY; INTESTINAL POLYP; LAXATIVES.

barium swallow A diagnostic imaging procedure to examine the structures of the upper gastrointestinal tract including the ESOPHAGUS, STOMACH, and DUODENUM (beginning of the SMALL INTESTINE), sometimes called an upper GI (gastrointestinal) series. The gastroenterologist may request a barium swallow to help diagnose HIATAL HERNIA, esophageal obstruction, ESOPHAGEAL SPASM, stomach dysfunction, and PEPTIC ULCER DISEASE. Preparation for barium swallow typically is nothing to eat or drink for 8 to 12 hours, before the procedure.

The test consists of swallowing a preparation of barium, a high-contrast medium, during a series of X-rays (FLUOROSCOPY). The barium lines the structures of the upper gastrointestinal tract, making them visible by X-ray. The barium preparation is about the consistency of a milkshake though chalky in texture. The procedure takes 30 to 60 minutes, with the person placed in different positions to help move the barium through the upper gastrointestinal tract. Some people experience mild CONSTIPATION after the procedure, and it is normal for the stools to be light-colored for several days after the procedure while the barium clears the body.

See also BARIUM ENEMA; ENDOSCOPY.

Barrett's esophagus Changes to the lining of the ESOPHAGUS in which the tissue becomes similar to that of the intestine. The altered tissue is Barrett's esophagus does not itself cause symptoms, though the condition often appears in association with GASTROESOPHAGEAL REFLUX DISORDER (GERD), which does cause symptoms. The key clinical significance of Barrett's esophagus is its association with a rare and deadly form of CANCER, esophageal ADENOCARCINOMA. Though few people who have Barrett's esophagus will develop esophageal adenocarcinoma, nearly everyone who does develop

esophageal adenocarcinoma also has Barrett's esophagus.

Diagnosis of Barrett's esophagus requires endoscopic biopsy of the esophageal lining. Altered tissue often appears reddened in endoscopic visualization, though appearance cannot make the diagnosis as GERD also can cause INFLAMMATION and irritation of the esophageal lining that causes it to appear reddened. A person who has confirmed Barrett's esophagus should undergo periodic endoscopic biopsy as a measure to detect further changes in the tissue (dysplasia) that could indicate a developing cancer. Esophageal adenocarcinoma appears to develop slowly, with a period of years during which the tissue changes are transitional. Dysplasia or cancer requires appropriate treatment, which varies according to individual health circumstances. There are no treatments for Barrett's esophagus or to prevent its conversion to esophageal adenocarcinoma.

See also CANCER RISK FACTORS; ENDOSCOPY; ESOPHAGEAL CANCER; ESOPHAGITIS.

bezoar A hardened mass of indigestible matter that forms in the STOMACH, such as HAIR (trichobezoar), insoluble plant fiber (phytobezoar), or a combination of hair and plant fiber (trichophytobezoar). Bezoars can develop in children who chew their hair or eat substances such as sand or grass and in adults who have slowed gastrointestinal motility, such as might occur with GASTROPARESIS or ACHALASIA. A bezoar can remain undetected in the stomach for months, until it becomes large enough to block the passage of food into the SMALL INTESTINE. Common symptoms include PAIN, NAUSEA, VOMITING, and occasionally a palpable lump. BARIUM SWALLOW or ENDOSCOPY can confirm the diagnosis. Surgery (endoscopic or open) to remove the bezoar is often the only treatment, as by the time a bezoar causes symptoms it is too large to pass through the gastrointestinal tract. Bezoars may recur when the behavior responsible for their development, such as hair chewing, persists.

See also ILEUS.

bile A liquid that the LIVER produces to carry some of its waste products into the digestive tract. Specialized cells called hepatocytes synthesize bile from water, cholesterol, bile acids, bile salts, BILIRUBIN and other bile pigments, and electrolytes. The hepatocytes break down cholesterol, a fatty acid, into bile acids. Other cells in the liver further convert bile acids into water-soluble forms called bile salts.

The SPLEEN is the body's scavenger and one of its jobs is to remove old erythrocytes (red BLOOD cells) from the blood and break them down. One of the byproducts of this process is heme, the iron compounds. After further metabolism one derivative of heme is bilirubin. Bilirubin is dark yellow and is the primary pigment in bile, giving bile its dominant yellow coloration. Other bile pigments come from substances the liver detoxifies from the blood, adding to the bile's color.

A network of BILE DUCTS collects bile from the liver and carries it to the GALLBLADDER. The walls of the gallbladder absorb about 90 percent of the water the bile contains, producing a greatly concentrated solution that the gallbladder ejects during digestion to aid in digesting fatty foods. Bile that enters the intestinal tract that the body does not need for digestion continues to travel through the intestines, eventually mixing with fecal matter for excretion from the body. The liver secretes about 750 milliliters (roughly a quart) of bile every day.

See also ERYTHROCYTE; CHOLESTEROL BLOOD LEVELS; GALLBLADDER DISEASE; PANCREATITIS.

bile ducts Channels that carry BILE from LIVER to the GALLBLADDER and from the gallbladder to the DUODENUM (first segment of the SMALL INTESTINE). The intrahepatic ducts are within the structure of the liver. They collect bile the liver secretes and transport it from the liver. The extrahepatic ducts are outside the liver and route bile to the gallbladder and duodenum. They are

- the hepatic duct, which carries bile out of the liver to the cystic duct
- the cystic duct, which carries bile from the hepatic duct to the gallbladder and from the gallbladder to the common duct
- the common duct, which carries bile into the duodenum

The health conditions most likely to involve the bile ducts are BILIARY ATRESIA, a CONGENITAL ANOMALY in which the bile ducts form incompletely or not at all, and ductal occlusion resulting from cholelithia-

sis, in which gallstones escape from the gallbladder and lodge in a bile duct, blocking the flow of bile and causing PAIN. CANCER of the bile ducts, called cholangiocarcinoma, occurs though is rare.

For further discussion of the bile ducts within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also GALLBLADDER DISEASE; PANCREAS; PRIMARY BILIARY CIRRHOSIS; PRIMARY SCLEROSING CHOLANGITIS.

biliary atresia Absence or malformation of the BILE DUCTS, also called neonatal CHOLESTASIS. Biliary atresia is nearly always congenital (present at birth). In some infants biliary atresia appears to develop as a consequence of an inflammatory process that occurs shortly after birth, destroying the bile ducts. Biliary atresia prevents the flow of BILE from the LIVER, causing toxins to accumulate in the liver. Symptoms depend on the extent of the atresia and may become apparent within days of birth or manifest slowly over the first six months of life. Symptoms include

- JAUNDICE, a yellowish discoloration of the SKIN resulting from the liver's inability to break down BILIRUBIN into components the body can excrete as waste
- stools that are pale in color, the consistency of clay, and unusually foul smelling
- dark URINE
- failure to grow or gain weight
- ABDOMINAL DISTENTION resulting from enlarged SPLEEN
- fussiness and irritability

NEONATAL JAUNDICE

NEONATAL JAUNDICE is fairly common, affecting about 50 percent of full-term and 80 percent of preterm (premature) newborns. It points to biliary atresia or other LIVER conditions only when it is apparent within the first 24 hours after birth or persists despite treatment.

The diagnostic path includes blood tests to measure the amounts of bilirubin in the blood and PERCUTANEOUS LIVER BIOPSY to determine whether the hepatocytes, the cells that process bilirubin, are normal. Normal hepatocytes strongly suggest biliary atresia. Other diagnostic procedures may include ULTRASOUND and intraoperative cholangiography (injecting dye into the bile ducts to visualize them using FLUOROSCOPY or other imaging technologies).

The only treatments for biliary atresia are surgical procedures to help restore the flow of bile. The first of these procedures is hepatic portoenterostomy, in which the surgeon creates an opening between the JEJUNUM (middle segment of the SMALL INTESTINE) and the bile duct structures that exist outside the liver. This procedure allows bile to drain directly from the liver into the small intestine and can achieve adequate liver function for up to several years. However, it does not correct the structural defects of the bile transport network within the liver, and damage to the liver (fibrosis and CIRRHOSIS) continues. Nearly all infants who have biliary atresia require LIVER TRANSPLANTATION, the second surgical procedure to treat the condition, before they are three years old. Long-term success of liver transplantation depends on numerous variables.

See also CONGENITAL ANOMALY; LIVER FAILURE.

bilirubin A metabolic product of ERYTHROCYTE (red BLOOD cell) heme that is a key component of HEMOGLOBIN. Bilirubin exists in two forms, conjugated (also called direct), which is water soluble, and unconjugated (also called indirect or free), which is fat soluble. The amounts and ratios of bilirubin present in the BLOOD help doctors assess LIVER and GALLBLADDER functions.

NORMAL BLOOD BILIRUBIN VALUES

unconjugated (indirect) bilirubin	0.1 to 1.0 milligrams per deciliter (mg/dL)
conjugated (direct) bilirubin	0.0 to 0.4 mg/dL
total bilirubin	0.3 to 1.9 mg/dL

The SPLEEN removes old erythrocytes (red blood cells), which contain high concentrations of hemoglobin, from the circulation and begins to break them down into their components. The bilirubin that results from this process is unconjugated, a form the body cannot eliminate. ALBUMIN, a protein in the blood, transports this unconjugated bilirubin to the liver. There, actions of an enzyme—glucuronyl transferase—help a chemical

reaction that converts the unconjugated bilirubin to conjugated bilirubin, which then becomes an ingredient of BILE.

Bilirubin is yellow and in turn colors the bile yellow; hence its designation as a bile pigment. Intestinal BACTERIA further metabolize bilirubin, the major component of which is urobilinogen. Urobilinogen gives the feces their characteristic dark color. Pale feces are a hallmark of disturbances of bilirubin METABOLISM. Increased bilirubin levels in the blood result in JAUNDICE, a yellowish discoloration of the SKIN most visible in the SCLERA ("white" of the EYE). Certain wavelengths of light on the skin help the body complete bilirubin metabolism.

See also CIRRHOSIS; HEPATITIS; PHOTOTHERAPY.

biliary dysfunction See GALLBLADDER DISEASE.

borborygmus The growling and rumbling sound of gas moving through the gastrointestinal tract during digestion. Borborygmus, sometimes referred to in the plural, *borborygmi,* indicates normal function of the gastrointestinal system. The sounds originate with the STOMACH and continue through the SMALL INTESTINE and large intestine. Excessive rumblings may indicate incomplete digestion such as may result from eating too rapidly or eating too much at one time. Some people experience an increase in borborygmus when they are hungry.

See also BOWEL SOUNDS; FLATULENCE.

bowel atresia A CONGENITAL ANOMALY in which there is incomplete development of the intestinal tract, typically with closures and "dead ends" that block flow through the intestines. The intestines may be entangled or intussuscepted (one segment of bowel telescopes into another), presenting grave risk for tissue death (necrosis). Nearly always the diagnosis is apparent within hours of birth because the infant is unable to eat and the abdomen quickly becomes distended. VOMITING BILE is a key indicator of intestinal obstruction of some sort. Bowel atresia is more common in premature infants. The most common locations for bowel atresia are the DUODENUM (duodenal atresia) and the JEJUNUM and ILEUM (jejunoileal atresia). Bowel atresia is life-threatening and requires emergency surgery to correct the defects.

See also ANAL ATRESIA; CONGENITAL HEART DISEASE; ESOPHAGEAL ATRESIA; INTUSSUSCEPTION.

bowel movement The passage of solid digestive waste (called feces or stool) from the body through the ANUS. The frequency, appearance, and nature of bowel movements are highly variable. Food typically travels through the gastrointestinal system in 18 to 36 hours, so most people have bowel movements daily or every other day. However, "normal" is an individual pattern that correlates to dietary habits, physical activity level, and lifestyle and can range from three bowel movements a day to one bowel movement every three days. What can become significant from a health standpoint are deviations from an individual's pattern of bowel movements. Short-term changes in bowel patterns may result from eating different foods, viral INFECTION (GASTROENTERITIS or ENTERITIS), inadequate fluid consumption, and medications. A shift in bowel patterns not due to intentional actions such as dietary or exercise change may indicate health conditions that require medical evaluation.

See also BOWEL SOUNDS; CONSTIPATION; DIARRHEA.

bowel sounds The noises of the gastrointestinal tract. Listening to bowel sounds through a stethoscope (AUSCULTATION) provides important clues about the function of the gastrointestinal tract. Normal bowel sounds vary in tone and loudness according to the activity of the bowel though follow characteristic patterns the doctor can identify. Excessive bowel sounds often accompany excessive bowel activity such as DIARRHEA, GASTROENTERITIS, and flare-ups of INFLAMMATORY BOWEL DISEASE (IBD). Reduced bowel sounds occur when bowel activity slows, such as between meals or when there is an intestinal obstruction. Narcotic medications and anesthetic agents also slow bowel function, and reduced bowel sounds may persist for several days after surgery. The absence of bowel sounds signals a nonfunctioning bowel, which can be due to intestinal obstruction or, in an infant, a gastrointestinal atresia. The absence of bowel sounds may be a sign of a medical emergency that requires surgical intervention.

See also BORBORYGMUS; BOWEL ATRESIA; ESOPHAGEAL ATRESIA.

C

cecum The first segment of the COLON (large intestine) into which the ILEUM, the final segment of the SMALL INTESTINE, empties digestive matter. The cecum is a pouchlike structure located in the lower right abdomen that absorbs water from the waste, returning fluid to the body and consolidating the waste for its journey through the end stage of digestion. The rhythmic contractions of PERISTALSIS move the remaining solid waste into the remainder of the colon. The APPENDIX extends from the bottom of the cecum.

For further discussion of the cecum and the colon within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also ANUS; RECTUM.

celiac disease A condition affecting the SMALL INTESTINE in which consuming foods that contain gluten, a plant protein prominent in wheat, triggers an inflammatory response that prevents the intestinal mucosa (lining) from absorbing NUTRIENTS. Gluten, and more specifically proteins it contains called gliadins, acts as an ANTIGEN to initiate a localized IMMUNE RESPONSE. Researchers believe celiac disease has a genetic foundation, though the specific GENE or genes responsible remain undetermined. Though severe celiac disease can cause significant NUTRITIONAL DEFICIENCIES that affect growth, FERTILITY, and overall health, most people who adopt a gluten-free diet are able to avert the inflammatory episodes and minimize damage to the intestinal mucosa. About 1 in 5,000 Americans has celiac disease.

Symptoms and Diagnostic Path

Symptoms appear in celiac disease with exposure to gluten, so usually do not become apparent until after the age of two years when children begin eating solid foods. People who have celiac disease experience a broad range of symptoms, with some people having virtually no indications they have celiac disease until nutritional deficiencies become problematic and other people suffering chronic DIARRHEA, cramping, ABDOMINAL DISTENTION, and other gastrointestinal disruptions. Some people have outbreaks of DERMATITIS herpetiformis, an itchy SKIN RASH. An early indication of celiac disease, especially in children, is the passing of large, loose, light-colored, foul-smelling stools, which suggests high fat excretion (STEATORRHEA) characteristic of MALABSORPTION.

Celiac disease may affect any or all of the segments of the small intestine, and the degree to which it affects them determines the symptoms. Many of the symptoms and signs of celiac disease arise from health problems due to nutritional deficiencies that correlate to the segment of small intestine affected, manifesting in conditions such as ANEMIA (deficiency of iron, suggesting involvement of the DUODENUM and upper JEJUNUM) and frequent nosebleeds (deficiency of VITAMIN K, suggesting involvement of the lower jejunum and the ILEUM). Children who have celiac disease may also appear malnourished, showing spindly limbs and protruding bellies, despite adequate food consumption.

Biopsy of the intestinal mucosa in people who have celiac disease tends to show marked structural differences from normal intestinal mucosa. Most significant is flattening of the mucosal tissue from its normal "pleated" appearance, which reduces the surface area available for nutrient absorption. Lymphocytes and leukocytes are also present within the mucosal tissue, evidence of the inflammatory process. However, there are no definitive tests to diagnose celiac disease. BLOOD

tests to measure ANTIBODY levels and biopsy of the intestinal mucosa provide strong, though not conclusive, evidence of celiac disease. Antibody levels become elevated only during active episodes of the disease, and biopsy samples may not represent the overall status of the small intestine.

The gastroenterologist considers these results in conjunction with the pattern of symptoms, FAMILY MEDICAL PEDIGREE, and response to a gluten-free diet. Symptoms that disappear with a gluten-free diet provide fairly conclusive diagnosis, though this marker is useful only in people who have obvious gastrointestinal or dermatologic symptoms.

Treatment Options and Outlook

The primary treatment for celiac disease is a gluten-free diet. This means eliminating all wheat and wheat products, as well as numerous processed foods that contain gluten as filler. Many foods that restaurants serve also contain gluten, requiring great diligence to determine food ingredients. Wheat-free products may still contain gluten. Some people also need to eliminate oats, barley, and rye and products made from them, as these grains contain small amounts of gluten. People who have severe celiac disease may require NUTRITIONAL SUPPLEMENTS or nutritional-replacement therapies. Most people who follow a gluten-free diet experience improvement within two weeks and an end to their symptoms within a few months. The longer there are no symptoms, the more the intestinal mucosa restores itself and often returns to normal in people who remain symptom-free for several years.

Risk Factors and Preventive Measures

Celiac disease appears to be genetic, and as yet researchers do not know what, if any, risk factors exist. Many people are able to control their symptoms and prevent disease flareups by avoiding foods that trigger them. The doctor also may recommend nutritional supplements to minimize or prevent nutritional deficiencies.

See also HUMAN LEUKOCYTE ANTIGENS (HLAS); INFLAMMATORY BOWEL DISEASE (IBD); IRRITABLE BOWEL SYNDROME (IBS); LEUKOCYTE; LYMPHOCYTE; MAJOR HISTOCOMPATABILITY COMPLEX (MHC); MALNUTRITION; MINERALS AND HEALTH; NUTRITIONAL NEEDS; VITAMINS AND HEALTH.

cholecystectomy A surgical OPERATION to remove the GALLBLADDER. Cholecystectomy is the most common treatment in the United States for GALLBLADDER DISEASE including gallstones (cholelithiasis), cholecystitis (INFLAMMATION or INFECTION of the gallbladder), and biliary dyskinesia (diminished ability of the gallbladder to eject BILE). About 500,000 Americans undergo cholecystectomy each year.

Surgical Procedure

There are two methods for performing cholecystectomy, laparoscopic and open. About 95 percent of cholecystectomies surgeons perform in the United States are laparoscopic. Surgeons perform open cholecystectomy, once the standard, only when there are contraindications for laparoscopic cholecystectomy (such as extreme OBESITY) or laparoscopic cholecystectomy cannot successfully remove the gallbladder (such as when there are many stones or there is extensive scarring from long-standing gallbladder disease or repeated infections). Both operations require general ANESTHESIA and an overnight stay in the hospital.

Laparoscopic cholecystectomy In laparoscopic cholecystectomy the surgeon makes four or five small incisions and inserts a laparoscope and tiny instruments through them. The surgeon operates by visualizing the gallbladder via closed-circuit television display. The operation takes 45 to 60 minutes. Most people then stay several hours in the recovery room and overnight in the hospital. After surgery, many people returning to regular daily activities (except strenuous physical exercise) within three weeks, though full recovery takes six to eight weeks.

Open cholecystectomy This procedure is major surgery. The surgeon makes an incision 5 to 8 inches long through the abdominal muscles to expose the LIVER and the gallbladder beneath it. The operation takes about two hours. Most people then stay five to seven days in the hospital. Many people can return to light activity in about four weeks. Full recovery after open cholecystectomy takes about 12 weeks.

Risks and Complications

The primary risks of either operation are bleeding, anesthesia reaction, damage to the bile ducts and other adjacent organs and structures, and postop-

erative infection. The surgeon often administers preoperative and postoperative doses of ANTIBIOTIC MEDICATIONS as a prophylactic measure for infection. Factors that can complicate or slow recovery include DIABETES, OBESITY, and bleeding or clotting disorders. For reasons doctors do not fully understand, 15 to 20 percent of people who undergo cholecystectomy (either laparoscopic or open) continue to experience symptoms similar to those of gallbladder disease even after surgery, called postcholecystectomy syndrome. Occasionally gallstones can escape from the gallbladder during surgery and become trapped in the common bile duct or cystic bile duct, requiring a follow-up procedure, typically ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP), to remove them. Rarely, gallstones can form in the bile ducts months to years after cholecystectomy.

Postoperative infection is a significant risk with open cholecystectomy and in people who have diabetes or obesity, as these conditions can impair HEALING. Warning signs of infection include

- increased PAIN at the incision site
- pain elsewhere in the abdomen
- drainage from the incision site
- FEVER (temperature above 101°F)
- NAUSEA and VOMITING

Prompt antibiotic therapy successfully treats most postoperative infections. Persistent infection or delayed treatment may result in an ABSCESS that requires additional surgery to open and drain the infection.

BENEFITS AND RISKS OF CHOLECYSTECTOMY

Benefits	Risks
ends symptoms	intraoperative or postoperative bleeding
restores normal digestion	ANESTHESIA reaction
averts symptom-related complications	postoperative PAIN
	postoperative INFECTION
	inadvertent damage to LIVER and other structures
	scarring and adhesions
	postcholecystectomy syndrome

Outlook and Lifestyle Modifications

Cholecystectomy eliminates symptoms in about 80 percent of people who have gallbladder disease. Most people return to the same lifestyle habits as before surgery, including eating. The liver continues to manufacture bile, which flows directly into the small intestine. The body adapts to the weaker concentration of this bile within a few weeks of the cholecystectomy, and digestion returns to normal. Some people find that high-fat meals generate mild to moderate gastrointestinal distress or mimic gallbladder disease symptoms for several months after surgery. People who undergo open cholecystectomy may be unable to participate in strenuous physical activities for up to six months while the abdominal muscles regain STRENGTH.

See also HEPATIC ABSCESS; JAUNDICE; SURGERY BENEFIT AND RISK ASSESSMENT.

cholecystitis See GALLBLADDER DISEASE.

cholelithiasis See GALLBLADDER DISEASE.

cholestasis Inadequate or lack of BILE flow resulting from either obstruction of the BILE DUCTS or dysfunctions of the LIVER. Common symptoms of cholestasis include

- JAUNDICE (yellow discoloration of the SKIN)
- PRURITUS (generalized itching)
- easy bruising
- pale stools and dark URINE
- xanthomas (fatty deposits in the dermis layer of the skin)

CONDITIONS THAT CAN CAUSE CHOLESTASIS

BILIARY ATRESIA	gallstones
HEPATITIS	HEPATOXINS
LIVER DISEASE OF ALCOHOLISM	medication SIDE EFFECTS
obstructed BILE DUCTS	PANCREATIC CANCER
PANCREATITIS	PRIMARY BILIARY CIRRHOSIS

The diagnostic path includes blood tests to confirm the cholestasis, typically the levels of BILIRUBIN and the enzyme alkaline phosphatase, both of which become elevated with cholestasis. Other diagnostic procedures may include ULTRASOUND,

COMPUTED TOMOGRAPHY (CT) SCAN, and PERCUTANEOUS LIVER BIOPSY. Treatment targets the underlying cause or condition.

Longstanding cholestasis can result in deficiencies of fat-soluble vitamins, notably vitamin D and VITAMIN K, as the SMALL INTESTINE needs bile to digest fats.

See also ALCOHOLISM; LIVER FAILURE; XANTHOMA.

cholesterol, endogenous A sterol ALCOHOL molecule essential for many functions of cellular METABOLISM and the synthesis (production) of numerous hormones. The LIVER synthesizes the cholesterol that circulates within the body (endogenous) from dietary fats, particularly saturated fats, and the components of dietary cholesterol that enter the bloodstream from the gastrointestinal tract. The liver can continue to synthesize cholesterol as long as it receives the ingredients to do so, under genetically mediated regulation.

Because cholesterol is fat soluble it does not dissolve in the blood, so lipoproteins bind with cholesterol to transport it through the bloodstream. Excessive amounts of cholesterol in the bloodstream contribute to cardiovascular conditions such as ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). Inadequate amounts of cholesterol in the body are uncommon though occur with conditions such as myelogenous LEUKEMIA and AIDS. Low cholesterol prevents cells from repairing themselves and also the body unable to produce "stress" hormones, such as CORTISOL that are essential for IMMUNE RESPONSE. The liver also uses cholesterol to synthesize BILE, which carries cholesterol into the gastrointestinal tract for reabsorption and recycling or elimination. Various endocrine glands use cholesterol to synthesize STEROID hormones, such as the ADRENAL GLANDS, which produce cortisol, and the gonads (sex glands), which produce TESTOSTERONE and ESTROGENS. Cells throughout the body use cholesterol for cell membrane repair.

See also CHOLESTEROL BLOOD LEVELS; CHOLESTEROL, DIETARY; HIV/AIDS; HYPERLIPIDEMIA; LIFESTYLE AND HEALTH; STRESS RESPONSE HORMONAL CASCADE.

cirrhosis A progressive condition in which fibrous tissue replaces damaged LIVER tissue, usually over an extended time and as a result of continued injury to the liver. The scarring is permanent and interferes with the liver's ability to function, eventually resulting in LIVER FAILURE. Numerous circumstances and health conditions can result in cirrhosis. The most common causes of cirrhosis are HEPATITIS, LIVER DISEASE OF ALCOHOLISM, chronic dysfunction of the BILE system, STEATOHEPATITIS, and HEPATOTOXINS. Cirrhosis is the leading reason for LIVER TRANSPLANTATION, the only treatment for end-stage cirrhosis and resulting liver failure.

Symptoms and Diagnostic Path

In its mild to moderate stages, cirrhosis often does not show symptoms or generates vague symptoms that suggest a variety of causes. Until cirrhosis becomes fairly advanced, even BLOOD tests that measure liver enzymes (a hallmark of liver function) and diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN often show normal findings. When symptoms become apparent, the cirrhosis has significantly compromised liver function, and numerous changes occur throughout the body. Indications of these changes often include

- edema (swelling of the limbs) and ASCITES (fluid accumulation in the abdominal cavity) resulting from PORTAL HYPERTENSION (increased resistance to blood flow through the liver) and RENAL FAILURE (kidney dysfunction)
- JAUNDICE (yellow discoloration of the SKIN) and PRURITIS (extreme itching of the skin) resulting from the liver's inability to metabolize HEMOGLOBIN and synthesize bile, which allows BILIRUBIN concentrations in the blood to rise
- easy bruising and prolonged bleeding due to the liver's inability to synthesize CLOTTING FACTORS and produce enough bile to metabolize the dietary fats necessary for absorbing VITAMIN K
- lack of APPETITE, resulting from diminished bile production, and corresponding unintended weight loss
- INSULIN RESISTANCE or type 2 DIABETES resulting from the liver's inability to properly metabolize cholesterol and manage GLUCOSE (sugar) storage and retrieval

- GYNECOMASTIA (enlarged breasts) in men and AMENORRHEA (absence of menstrual periods) in women due to the diminished ability of the liver to metabolize ESTROGENS

The liver may feel enlarged or irregular when the gastroenterologist palpates the abdomen. By this stage, numerous blood chemistry tests show abnormal results. PERCUTANEOUS LIVER BIOPSY confirms the presence of fibrous tissue and the diagnosis of cirrhosis.

Treatment Options and Outlook

Treatment attempts to manage symptoms, address consequential health problems, and slow the progression of any underlying health conditions. Eliminating ALCOHOL consumption, medications, and environmental exposures that damage liver cells are among the measures essential to preserve remaining liver function. Numerous clinical studies show the ability of the herbal product MILK THISTLE or silymarin, its active ingredient, to help protect the liver from further damage. When cirrhosis progresses despite these interventions, liver transplantation becomes the treatment of final resort. Without liver transplantation, progressive cirrhosis is fatal. Liver transplantation permanently resolves cirrhosis, though at present there are far fewer donor livers available than people who need them. Live donor liver segment donation, in which a living person donates a portion of his or her healthy liver, is an option to full liver transplantation when a donor is available.

Risk Factors and Preventive Measures

Cirrhosis results from chronic, long-term damage to the liver. People who are at risk for developing cirrhosis have longstanding liver disease, such as chronic hepatitis, hepatitis of ALCOHOLISM, HEMOCHROMATOSIS, PRIMARY BILIARY CIRRHOSIS, PRIMARY SCLEROSING CHOLANGITIS, and WILSON'S DISEASE. Preventive measures include vaccination against hepatitis INFECTION (hepatitis A and hepatitis B) and minimizing behaviors that allow exposure to hepatitis. Consistent PERSONAL HYGIENE practices, such as HAND WASHING before handling food and after going to the bathroom, help control the spread of the hepatitis VIRUS.

See also HEPATITIS PREVENTION; LIFESTYLE AND HEALTH; ORGAN TRANSPLANTATION.

colitis INFLAMMATION of the COLON. Colitis can be acute (sudden) or chronic (long-term). Various circumstances can cause acute colitis. Among them are INFECTION, radiation, and ischemia. Chronic colitis is usually a form of INFLAMMATORY BOWEL DISEASE (IBD), an autoimmune disorder. The symptoms of colitis are abdominal discomfort, cramping, and DIARRHEA. The doctor makes the diagnosis primarily on the basis of symptoms; BLOOD tests often can confirm the presence of pathogens. Treatment may include medications that target the underlying cause of the inflammation or infection as well as antidiarrheal medications.

Infectious Colitis

Bacterial and protozoan infections of the colon are common. People who are already debilitated—such as the very old, the very young, and those with compromised immune function—face increased risk for complications, such as DEHYDRATION, that can be fatal. Fecal cultures can identify the causative agent, which then determines the appropriate treatment.

Bacterial colitis Numerous BACTERIA cause bacterial infections of the colon, which often are FOODBORNE ILLNESSES. Those most frequently detected include *Salmonella, Shigella, Campylobacter jejuni,* and *Listeria monocytogenes*. Treatment for bacterial colitis is the appropriate antibiotic medication, which helps contain symptoms within 48 to 72 hours and eliminate the infection in about 10 to 14 days. Bacterial infections, notably LISTERIOSIS, can be especially dangerous for pregnant women.

Parasites Parasitic infections can occur from drinking contaminated water, eating contaminated foods, and through contact with someone who has such an infection. It is possible to have a protozoan or parasitic infection and show no symptoms. The most common infective protozoan is *Entamoeba histolytica*, which causes AMEBIASIS (also called amoebic dysentery). Treatment is a course of antiparasitic medication such as metronidazole. Recovery is usually complete with appropriate treatment. Other protozoan infections include GIARDIASIS, CYCLOSPORIASIS, and CRYPTOSPORIDIASIS.

Radiation Colitis

RADIATION THERAPY to treat cancers, such as PROSTATE CANCER, in the lower abdominal region

(pelvic area) can damage the colon, causing symptoms such as diarrhea and cramping. Symptoms typically resolve as the damaged tissue regenerates. Treatment targets symptom relief. Radiation colitis typically resolves when radiation therapy ends.

Ischemic Colitis

Impaired blood flow to the intestinal tract, such as might occur with serious ATHEROSCLEROSIS, can impede intestinal function. Ischemic colitis is most common in people age 70 and older. Treatment focuses on restoring adequate circulation and minimizing symptoms, such as diarrhea, that can result in nutritional deficits and dehydration.

Inflammatory Bowel Disease (IBD)

Chronic inflammation of the colon takes the form of ulcerative colitis or Crohn's disease, collectively called IBD. Crohn's disease can affect the entire gastrointestinal tract but most commonly involves the terminal ileum and the ascending colon. Ulcerative colitis can affect the whole colon but usually starts in the rectum and left colon. IBD is an autoimmune disorder in which the IMMUNE SYSTEM attacks sections of the intestinal tract and destroys the mucus lining. This creates ulcerations that cause PAIN, diarrhea, and MALABSORPTION. Treatment for inflammatory colitis typically includes CORTICOSTEROID MEDICATIONS and sometimes immunosuppressive agents such as methotrexate or cyclosporine to suppress the IMMUNE RESPONSE. IBD is a serious and lifelong disorder that requires continuous management through medications and diet.

See also ANTIBIOTIC MEDICATIONS; AUTOIMMUNE DISORDERS; ENTERITIS; FOOD SAFETY; GASTRITIS; GASTROENTERITIS; INCUBATION PERIOD; IRRITABLE BOWEL SYNDROME (IBS); NUTRITIONAL NEEDS; NUTRITIONAL SUPPLEMENTS; PATHOGEN; PERSONAL HYGIENE; PROCTITIS; VIRUS; WATER SAFETY.

colon The large intestine, which extracts water from and consolidates the waste byproducts of digestion. The colon extends from the ILEUM, the final segment of the SMALL INTESTINE, to the ANUS, the exit from the body for solid digestive waste (feces or stool). The colon goes up the left side of the abdomen (the ascending colon), across the abdomen at the lower ribs (the transverse colon), and down the right side of the abdomen to about the level of the hip JOINT (the descending colon). The final segments of the colon are the sigmoid colon and the RECTUM. The colon is about five feet long in the average adult.

COMMON CONDITIONS AFFECTING THE COLON

COLITIS	COLORECTAL CANCER
CONSTIPATION	Crohn's disease
DIARRHEA	DIVERTICULAR DISEASE
FECAL IMPACTION	FECAL INCONTINENCE
HIRSCHSPRUNG'S DISEASE	ILEUS
INFLAMMATORY BOWEL DISEASE (IBD)	INTESTINAL POLYP
IRRITABLE BOWEL SYDROME (IBS)	PROCTITIS
RECTAL FISTULA	RECTAL PROLAPSE
TOXIC MEGACOLON	ulcerative colitis

For further discussion of the colon within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also ANAL ATRESIA; ANAL FISSURE; BORBORYGMUS; BOWEL ATRESIA; BOWEL SOUNDS; COLONOSCOPY; STOMACH.

colonoscopy An examination of the COLON (also called bowel or large intestine) to detect and remove INTESTINAL POLYPS, fleshy growths that may become cancerous, and to biopsy or remove small adenocarcinomas (cancerous polyps). Conventional colonoscopy is an endoscopic procedure in which the gastroenterologist inserts a flexible, lighted tube (endoscope or colonoscope) through the ANUS and into the large intestine.

Reasons for Doing This Test

Colonoscopy is a diagnostic procedure to detect intestinal polyps, COLORECTAL CANCER, and other conditions affecting the colon. Cancer experts believe screening colonoscopy, performed at age 50 (or earlier, when there is family history of colorectal cancer) and every 5 to 10 years thereafter, can prevent 80 to 90 percent of colorectal cancers.

Preparation, Procedure, and Recovery

The gastroenterologist performs conventional colonoscopy in an ENDOSCOPY center or hospital unit, with intravenous general sedation to mini-

mize discomfort and anxiety. The procedure takes 30 to 45 minutes, with another one to two hours to recover from the sedation.

Preparation Most people find the preparation for colonoscopy, which consists of cleansing the gastrointestinal tract, the most unpleasant aspect of the procedure. The preparation for virtual colonoscopy requires the same bowel-cleansing procedure as does conventional colonoscopy. Completing the preparation for colonoscopy is essential for optimal results, however. It typically includes

- no aspirin or aspirin products (to reduce the risk for bleeding) and no iron supplements or products (iron darkens tissue) for five days before the colonoscopy
- no nuts, seeds, grapes, peas, beans, or tomatoes for three days before the colonoscopy (particles from these foods lodge in the folds of the intestinal mucosa)
- no NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) for five to seven days before the colonoscopy (to reduce the risk for bleeding)
- only clear liquids for 24 hours before the colonoscopy
- at midday the day before the colonoscopy, the bowel-cleansing process begins with the drinking of a laxative solution consumed at the rate of eight ounces every 10 minutes for a total consumption of one gallon of the solution

The laxative prep results in bowel movements that start about an hour after beginning to drink the solution and continue for about eight hours. Drinking the solution often causes NAUSEA. Keeping the solution as cold as possible (even surrounding it with ice in the refrigerator) and chewing gum or sucking on hard candy between glasses can help. It is necessary to drink the entire gallon of the solution to completely clear the gastrointestinal tract. Fecal remnants in the colon can obscure the wall of the bowel, limiting the ability of the gastroenterologist to visualize the entire colon. Most gastroenterologists will not proceed with the colonoscopy if the preparation is incomplete.

Procedure The person lies on his or her left side on a narrow bed, with the knees flexed. After initiating intravenous sedation, the gastroenterologist gently inserts the lubricated colonoscope into the anus. A small pump injects air ahead of the scope, opening the colon so the gastroenterologist can advance it into the colon. The examination of the colon takes about 20 minutes, longer when there are polyps for the gastroenterologist to remove or biopsy. Some people feel pressure with the injection of air or when the scope rounds the corners of the colon. However, most people feel little discomfort and cannot recall the procedure when it is over.

Recovery Following conventional colonoscopy, the person rests in a recovery area until the sedative wears off, usually within an hour or two, and then may go home. Doctors recommend resting quietly for the remainder of the day, which is what most people feel like doing. There is usually no discomfort after the procedure, aside from an accumulation of intestinal gas until regular eating returns the gastrointestinal tract to normal function. The gastroenterologist receives the pathologist's analysis of any tissues removed within about a week. Following virtual colonoscopy, the person may go home immediately after the procedure.

Risks and Complications

Complications related to conventional colonoscopy are very rare but may include perforated bowel (which requires emergency surgery to repair), INFECTION, and bleeding from removed or biopsied polyps.

Virtual Colonoscopy

Virtual colonoscopy, a procedure that allows noninvasive visualization of the gastrointestinal tract, became available in the late 1990s. Virtual colonoscopy, correctly called computed tomography colonography or CT colonography, uses COMPUTED TOMOGRAPHY (CT) SCAN to examine the colon with nearly the same accuracy as conventional colonoscopy but without the need for sedation or to enter the body.

The significant drawback to CT colonography is that it allows only viewing of the colon, not biopsy or polypectomy. The gastroenterologist must still use conventional colonoscopy to remove detected intestinal polyps or to biopsy suspicious growths. The preparation for virtual colonoscopy

requires the same bowel cleansing procedure as does conventional colonoscopy.

Virtual colonoscopy does not require sedation. For the procedure, the radiologist inserts a small tube into the rectum for the injection of air to open the colon for improved visualization, which may cause discomfort that feels like intestinal gas. Over a period of 10 to 20 minutes the CT scanner takes sequential X-rays while the person lies on his or her back and then STOMACH. A computer compiles the X-rays to create three-dimensional images of the colon.

See also BARIUM ENEMA; CANCER PREVENTION; INTESTINAL POLYP.

colorectal cancer Malignant growths in the COLON, most commonly in the sigmoid colon and the RECTUM. Colorectal cancer is the second-leading cause of death due to CANCER in the United States. However, colorectal cancer is also one of the most preventable and, with early detection, among the most treatable kinds of cancer. More than 95 percent of primary colorectal cancer is ADENOCARCINOMA, a form of cancer in which abnormal but otherwise benign growths (adenomas) become cancerous. Intestinal polyps are adenomas that develop in the colon, growing from the mucous membrane that lines the colon. Intestinal polyps become more common with increasing age, and by age 50, about half of American adults are likely to have them.

TYPES OF POLYPS

There are two common types of colon polyps: adenomas, which are neoplastic (abnormal growths that have no useful function within the body) and have malignant potential, and hyperplastic, which are not neoplastic and have no malignant potential.

A polyp takes 5 to 10 years to grow from microscopic to detectable, and up to several decades to become cancerous, if that is its course. People who have no exceptional risk factors for colorectal cancer typically have a window of 5 to 10 years during which the polyp's cell structure is transitional. Doctors consider such a polyp precancerous. Though only a small percentage of intestinal polyps will become cancerous, there is no way to distinguish those that will from those that will remain benign. As a precaution doctors recommend removing all intestinal polyps, which eliminates any concerns about their potential malignancy.

Symptoms and Diagnostic Path

Early colorectal cancer has few, if any, symptoms, further emphasizing the importance of regular screening. When present, symptoms often indicate a cancer that is moderately to significantly advanced and include

- a change in bowel habits or the nature of bowel movements
- unexplained NAUSEA, VOMITING, DIARRHEA, or CONSTIPATION
- rectal bleeding (may be patches of dark discoloration or bright bleeding)
- sensations of abdominal fullness or bloating
- tiredness and fatigue
- unintended weight loss
- ABDOMINAL DISTENTION and pain

The most effective way to detect and diagnose colorectal cancer is through regular screening procedures, which may include

- DIGITAL RECTAL EXAMINATION (DRE), in which the doctor inserts a gloved, lubricated finger into the rectum via the ANUS to feel for abnormalities
- FECAL OCCULT BLOOD TEST (FOBT), in which a laboratory tests a stool sample for microscopic blood (home-testing kits are also available)
- double-contrast BARIUM ENEMA, in which the radiologist instills barium into the lower colon via an ENEMA, then takes X-rays as the barium fills the rectum and sigmoid colon
- sigmoidoscopy, in which the doctor inserts a lighted viewing tube (rigid or flexible) through the anus into the rectum and sigmoid colon, the two segments of the colon nearest the end of the intestinal tract and the sites where more than half of colorectal cancers originate
- COLONOSCOPY, in which the doctor inserts a lighted, flexible viewing tube through the anus and into the entire colon (done under sedation)
- virtual colonoscopy (CT colonography)

Sigmoidoscopy (for the lower colon) and colonoscopy (for the full length of the colon) allow the gastroenterologist to detect and remove intestinal polyps and to biopsy suspicious growths. The gastroenterologist may use colonoscopy to explore suspicious findings from other screening procedures. Further diagnostic procedures may include transrectal or abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI).

Pathology examination of the suspect tissue confirms the diagnosis and establishes the extent of the cancer, a clinical classification process called STAGING OF CANCER. Staging identifies how far the cancer has spread, determines treatment recommendations and protocols, and establishes expectations about how the cancer will respond to treatment (prognosis). The higher the stage number, the more advanced the cancer.

Treatment Options and Outlook

Surgery is the first course of treatment for nearly all colorectal cancers. In cancers detected early, surgery often cures the cancer. Depending on the location and extent of the cancer, the surgeon can usually remove the cancerous tissue (called a bowel resection) and reconnect the healthy ends of the colon so the colon continues to function normally. Sometimes the colon needs first to heal from the resection, in which case the surgeon performs a temporary COLOSTOMY that allows the colon to pass fecal matter through an opening created in the abdomen. When the colon heals, the surgeon reconnects the ends and closes the colostomy. Extensive cancer may make necessary a permanent colostomy.

The oncologist may recommend RADIATION THERAPY to shrink large tumors before surgery or to kill any cancerous cells remaining after surgery, primarily for cancer located in the rectum. CHEMOTHERAPY kills cancer cells that may have spread beyond the local tumor, and is the follow-up treatment of choice for cancers that involve LYMPH NODES. Often the oncologist will recommend a combination of therapies. Oncologists also typically offer people who have stage 2 through stage 4 colorectal cancer the opportunity to participate in clinical research studies of new treatments. It is important to fully understand the benefits and risks of the investigational treatment.

BASIC STAGING OF COLORECTAL CANCER

Stage	Meaning	Treatment Protocol
stage 0	cancer is in its earliest stages, completely confined to the polyp; also called CARCINOMA in situ or intramucosal carcinoma	surgery to remove the cancerous polyp (polypectomy), typically via COLONOSCOPY
stage 1	cancer involves but remains confined to the inner layers of the intestinal mucosa	surgery to remove the tumor and the involved segment of colon (local excision)
stage 2	cancer extends beyond the wall of the COLON but not into the LYMPH NODES	surgery to remove the tumor and involved segment of colon; occasionally RADIATION THERAPY or CHEMOTHERAPY
stage 3	cancer extends beyond the wall of the colon and into nearby lymph nodes	surgery to remove the tumor, the involved segment of colon, the surrounding tissue into which the cancer has spread, and the involved lymph nodes; radiation therapy or chemotherapy
stage 4	cancer has spread to other organs	surgery to remove tumors and involved tissues when possible; radiation therapy and/or chemotherapy
recurrent	a return of the cancer to the colon	surgery to remove the tumor and involved segment of colon; radiation therapy and/or chemotherapy

Treatments for cancer offer varying benefits and risks. Cancer experts often recommend obtaining a second opinion evaluation from another physician specialist before making treatment decisions. Treatment is highly successful for colorectal cancers detected before they spread beyond the wall of the bowel. Stage 0 colorectal cancer is nearly always curable, and more than 90 percent of people diagnosed with stage 1 colorectal cancer are cancer-free five years after treatment. The course of advanced and recurrent colorectal cancer is more challenging, and often results in moderate to significant lifestyle changes. Recovery from extensive surgery may take several months, and radiation therapy and chemotherapy typically cause numerous and varied side effects that often limit participation in regular activities. Though the outlook for colorectal cancer continues to improve with early detection and new treatment technologies, it remains a serious health condition that requires appropriate and

COLORECTAL CANCER SCREENING PROCEDURES

Procedure	Frequency	Benefits	Drawbacks or Risks
DIGITAL RECTAL EXAMINATION (DRE)	annually after age 45	can detect growths and abnormalities in the RECTUM	does not detect very small growths or growths beyond the rectum further procedures required to investigate positive results
FECAL OCCULT BLOOD TEST (FOBT)	annually after age 50	detects microscopic blood in the stool, often while the growth causing the bleeding is still very small; sample collected at home; home-testing kits available	the growth is large enough to cause bleeding by the time of detection compliance is low further procedures required to investigate positive results
sigmoidoscopy	every 5 years for those with average risk; every 3 years for those with increased risk	provides direct examination of the walls of the rectum and sigmoid COLON; doctor can remove or biopsy detected polyps or tumors	does not visualize full length of the colon unpleasant preparation some discomfort during the procedure minimal risk of INFECTION, bleeding, or perforation further procedures required to investigate positive results
double-contrast BARIUM ENEMA	every 10 years for those with average risk; every 5 years for those with increased risk	provides clear representation of the full colon	does not detect very small polyps or tumors less effective in detecting polyps or tumors in the rectum than in the colon unpleasant preparation some discomfort during the procedure further procedures required to investigate positive results
COLONOSCOPY	every 10 years for those with average risk; every 5 years for those with increased risk	allows direct examination of the full colon; doctor can remove or biopsy detected polyps or tumors	unpleasant preparation some discomfort during the procedure requires general sedation minimal risk of infection, bleeding, or perforation

diligent attention. Cancer SUPPORT GROUPS provide excellent opportunities to share experiences and feelings in a protected setting.

Risk Factors and Preventive Measures

The most significant risk factor for colorectal cancer, as for many kinds of cancer, is age. Doctors diagnose more than 90 percent of colorectal cancer in people who are age 50 and older. Health and medical factors that present increased risk include

- of early-onset (before age 50) colorectal cancer among first-degree family members, notably parents and siblings
- previous diagnosis of colorectal cancer
- previous diagnosis of BREAST CANCER, endometrial (uterine) cancer, or OVARIAN CANCER in women
- mutations of the adenomatous polyposis coli (APC) gene, which causes FAMILIAL ADENOMATOUS POLYPOSIS (FAP), or of the gene that causes HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC); both mutations are rare, together accounting for less than 3 percent of colorectal cancers
- INFLAMMATORY BOWEL DISEASE (IBD), which may feature Crohn's disease, ulcerative COLITIS, or both
- OBESITY, notably ABDOMINAL ADIPOSITY (excess body fat carried around the belly)

Lifestyle factors that appear to increase the risk for colorectal cancer include a diet high in saturated fats (animal-based fats) and low in fruits and vegetables, lack of daily physical exercise, and smoking.

Regular screening is the most effective preventive measure for colorectal cancer. Cancer experts recommend colonoscopy as the first line of screening for colorectal cancer in most people starting at age 50, though earlier in people with family members who have had colorectal cancer at an earlier age, every 10 years for people with average risk and every 5 years for people with additional risk factors. Research suggests such screening could eliminate 80 to 90 percent of colorectal cancer.

Though conclusive evidence of dietary correlations to risk for intestinal polyps and colorectal cancer remains elusive, cancer experts encourage a diet high in natural fiber (especially fresh fruits and vegetables) and low in saturated fat. Other lifestyle recommendations include daily physical exercise, SMOKING CESSATION, and weight management.

See also ADENOMA-TO-CARCINOMA TRANSITION; CANCER PREVENTION; CANCER RISK FACTORS; CANCER TREATMENT OPTIONS AND DECISIONS; DIET AND HEALTH; END OF LIFE CONCERNS; FIBER AND GASTROINTESTINAL HEALTH; INTESTINAL POLYP; SMOKING AND HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT; WEIGHT LOSS AND WEIGHT MANAGEMENT.

colostomy A surgically created opening (stoma) through the abdominal wall through which the COLON passes fecal matter, typically accompanying surgery to remove a diseased segment of the colon. Though there are numerous medical reasons for colostomy, among the most common are COLORECTAL CANCER, traumatic injury, and severe INFLAMMATORY BOWEL DISEASE (IBD). A colostomy may be temporary when a period of nonactivity will help the colon recover from INFECTION or inflammatory damage or during the stages of reconstructive surgery. A colostomy is likely to be permanent when the surgeon must remove large segments of bowel.

The OPERATION is a major surgery done under general anesthetic. Typically the person enters the hospital the night before the scheduled OPERATION to complete the preparations for surgery, which usually include LAXATIVES and enemas to thoroughly cleanse the colon. The length of the operation depends on the extent of the procedures. The surgeon attempts to locate the colostomy in the lower abdomen when possible, though may place a temporary colostomy in the upper abdomen to rest the lower segments of the colon. Most people remain in the hospital for five to seven days, during which time an ostomy-care specialist provides education and instruction about colostomy care. HEALING after surgery takes about six to eight weeks. Diligent WOUND CARE during this period is essential to reduce the risk for infection and irritation and to help the stoma heal properly.

A small plastic bag, sealed against the SKIN with adhesive around the opening (stoma), collects fecal matter that exits the colon through the

colostomy. It is important to empty or change the colostomy bag frequently and regularly and to cleanse the skin around the stoma with each changing to minimize irritation from the adhesive and from fecal matter. Frequent bag changes also reduce odor, as do deodorizing tablets that go into the ostomy bag. Over time, most people find that certain foods (such as meats and many processed foods) are more likely than others to cause odor or irritation and can avoid eating them to further reduce odor.

Concerns about how having a colostomy will change appearance and daily living activities are natural and common. A colostomy significantly alters the body's structure and excretory function, which many people find challenging. An ostomy-care specialist can provide information and suggestions to smooth the adjustment. Most people find they are able to return to their regular activities when the stoma fully heals. The colostomy should not interfere with clothing, exercise, lifting and carrying, and most other daily activities.

The effect of colostomy on SEXUALITY is a major concern for most people. A risk of surgery on the colon is damage to the nerves that supply the perineal area, which can result in altered sensations in men and women and ERECTILE DYSFUNCTION in men. Some people feel self-conscious or embarrassed about having a colostomy. However, many people who have colostomies can return to regular sexual activity as soon as they feel the desire to do so. A special cap can cover the stoma during sex. Having SEXUAL INTERCOURSE or ORGASM does not cause any harm to the colostomy or adversely affect the underlying condition in most circumstances. It is important for partners to discuss their concerns and feelings openly and honestly so they can maintain intimacy within their relationships.

See also ILEOANAL RESERVOIR; ILEOSTOMY.

constipation Difficult or delayed bowel movements. Constipation may occur as a delay in the frequency of bowel movements, an attempt to pass stools that are hard and compact, or a combination. Constipation tends to be chronic (long-term), though can occur as acute (sudden) episodes. Abdominal cramping and bloating may accompany constipation.

Any rectal bleeding that accompanies constipation or bowel movements requires medical evaluation.

Though constipation can signal serious health conditions such as intestinal obstruction or HYPOTHYROIDISM, most often constipation relates to lifestyle factors such as diet, physical exercise, and HYDRATION (fluid intake). Numerous medications, notably ANTIHISTAMINE MEDICATIONS, narcotic ANALGESIC MEDICATIONS (pain relievers) and ANTIDEPRESSANT MEDICATIONS, can cause constipation. Constipation becomes more common with increasing age, partly due to lifestyle factors and partly due to age-related changes in intestinal motility.

Stools become hardened when the COLON extracts too much water from the fecal matter that passes through it. This can occur because the body needs more fluid (inadequate fluid intake) or because the fecal matter spends too much time in the colon (a consequence of inactivity or decreased intestinal motility). Hardened stools are difficult to pass and may cause irritation and even ABRASIONS to the anal canal and ANUS. Straining with the effort of a difficult BOWEL MOVEMENT aggravates common conditions such as HEMORRHOIDS and can have cardiovascular consequences such as ARRHYTHMIA (irregular heartbeat). Long-term use of LAXATIVES causes the colon to become reliant on them to stimulate bowel movements; overuse of laxatives is a frequent cause of chronic constipation.

For occasional constipation, many doctors recommend home treatment for two to three weeks, consisting of:

- increased water consumption
- increased fiber in the diet (eating more vegetables, fruits, whole grains, and whole grain products)
- 45 minutes to an hour of daily physical exercise such as walking, which encourages PERISTALSIS (the rhythmic, wavelike contractions of the intestinal wall) and improves BLOOD flow
- no laxatives
- sitz baths and hemorrhoidal preparations to soothe irritated hemorrhoids

These measures facilitate a return to gastrointestinal regularity for most people. Constipation that extends beyond two or three weeks, occurs with rectal bleeding, or causes ABDOMINAL PAIN or ABDOMINAL DISTENTION requires prompt medical evaluation.

See also AGING, GASTROINTESTINAL CHANGES THAT OCCUR WITH; ANAL FISSURE; DIARRHEA; FECAL IMPACTION; FECAL INCONTINENCE; FIBER AND GASTROINTESTINAL HEALTH; SITZ BATH.

Crohn's disease See INFLAMMATORY BOWEL DISEASE (IBD).

cyclic vomiting syndrome Episodes of uncontrolled VOMITING and NAUSEA, sometimes called abdominal migraine, that occur in cycles of symptoms and relief. Each episode may last hours and often repeats over a period of time after which there is an extended period without symptoms. Many people experience prodrome, a short period of time during which they have nausea, ABDOMINAL PAIN, a sense of the impending episode, or other symptoms that consistently occur before an episode. During an active episode, the person has persistent nausea and repeated vomiting that can last for hours to days.

Researchers believe the physiologic mechanisms of cyclic vomiting syndrome are similar to those of migraine headaches. Episode triggers may include infections and other physiologic stress, emotional stress, and certain foods such as chocolate. There are no conclusive diagnostic markers or tests for cyclic vomiting syndrome, making diagnosis a challenge. Generally the gastroenterologist strives to rule out other conditions that could cause the symptoms, resulting in diagnosis by exclusion.

Treatment targets symptom relief to the extent possible, which for many people is minimal, and supportive measures such as drinking plenty of fluids to replace those lost through vomiting. Some people experience relief with medications intended to head off migraine HEADACHE. Though some people can avert active episodes with medications or by altering their activities during the prodrome stage, there are no certain methods for preventing episodes. There is no known cure for cyclic vomiting syndrome, though episodes often diminish with aging. Cyclic vomiting syndrome is more common in children than adults, and can manifest in children as young as two or three years old.

See also GASTROENTERITIS.

D

diarrhea Watery or frequent bowel movements. Diarrhea can have serious health consequences for the very young, the very old, and those who have debilitating illnesses. It is important to increase fluid consumption when diarrhea is present as DEHYDRATION can occur very quickly. Diarrhea in an infant under six months old requires immediate medical attention. For older children and adults, medical attention becomes necessary when diarrhea exists with:

- ABDOMINAL PAIN for longer than two hours
- FEVER above 101°F for longer than 24 hours
- profuse VOMITING
- reduced or lack of URINATION
- suspected ingestion of toxic or obstructive substance

Bloody diarrhea may signal a serious health condition and requires immediate medical evaluation.

Numerous causes exist for diarrhea. Foods containing table sugar (sucrose), sugars that occur in milk (lactose), fruits (fructose), and sweeteners in juices and soft drinks (sorbitol and mannitol) can cause or worsen diarrhea because they draw additional fluid into the large intestine. Viral, bacterial, and parasitic infections, often food-borne, are common causes of diarrhea. Diarrhea is also a common symptom with gastrointestinal disorders such as IRRITABLE BOWEL SYNDROME (IBS) and INFLAMMATORY BOWEL DISEASE (IBD). Extended periods (weeks to months) of loose or frequent bowel movements may suggest dysfunction of the SMALL INTESTINE or MALABSORPTION disorders. Frequent, small bowel movements that are a change from usual bowel patterns may indicate conditions of the large intestine such as intestinal polyps or COLORECTAL CANCER. Women may have mild diarrhea with their menstrual periods. Diarrhea may occur with changes in eating habits, such as when traveling.

COMMON CAUSES OF DIARRHEA

antibiotic therapy	CELIAC DISEASE
changes in EATING HABITS	COLORECTAL CANCER
DIVERTICULAR DISEASE	excessive ALCOHOL consumption
excessive CAFFEINE consumption	FOOD-BORNE ILLNESSES
foods and beverages	GALLBLADDER DISEASE
ILEUS	INFLAMMATORY BOWEL DISEASE (IBD)
ingested toxins	INTESTINAL POLYP
IRRITABLE BOWEL SYNDROME (IBS)	MALABSORPTION
medication SIDE EFFECTS	viral, bacterial, and parasitic INFECTION

Bland foods such as cooked rice, oatmeal, soda crackers, graham crackers, and bananas can help calm the gastrointestinal tract and restore normal bowel function. Doctors often recommend an oral rehydration solution (ORS) such as Pedialyte or Rehydralyte when diarrhea persists beyond a few days in children, and for adults who show indications of dehydration or have extensive diarrhea. Doctors may recommend ANTIDIARRHEAL MEDICATIONS such as loperamide (Imodium) that slow PERISTALSIS (intestinal movement) to help control symptoms. Most diarrhea, though disruptive, represents minor and temporary gastrointestinal disturbance that fully resolves within one to three weeks.

See also COLITIS; GASTROENTERITIS; FOOD SAFETY.

digestive enzymes Specialized protein structures that help break down (hydrolyze) foods in the

MOUTH, STOMACH, and SMALL INTESTINE to assist in absorbing NUTRIENTS from foods. Gastrointestinal structures produce dozens of digestive enzymes, which they secrete in various digestive juices. Amylase in saliva, for example, breaks down carbohydrates into their sugar components. Gastric juices combine acid and protease (pepsin) to further hydrolyze foods. Numerous enzymes in the small intestine—such as lactase, cellulase, lipase, maltase—facilitate the chemical changes necessary to convert food particles to nutrient molecules the intestinal mucosa can absorb and transport into the bloodstream. Shortages of enzymes may occur, naturally or due to health conditions, that result in gastrointestinal disorders. A shortage of lactase, for example, causes LACTOSE INTOLERANCE.

See also CARBOHYDRATE INTOLERANCE; DIGESTIVE HORMONES; NUTRITIONAL SUPPLEMENTS.

digestive hormones Chemical messengers that stimulate or inhibit gastrointestinal functions. Organs and structures of the gastrointestinal system synthesize and release digestive hormones in response to chemical and physiologic changes that take place with the ingestion of food and its passage through the gastrointestinal tract. The major digestive hormones are

- gastrin, which stimulates the STOMACH to release gastric juices and begin contracting
- cholecystokinin (CCK), which stimulates the GALLBLADDER to release BILE, the PANCREAS to release digestive juices, and the stomach to slow the release of chyme (the slushy mix of food and digestive secretions) into the DUODENUM (first segment of the SMALL INTESTINE)
- secretin, which accelerates bile release from the gallbladder, stimulates the pancreas to release bicarbonates to neutralize stomach acid, and slows the release of gastric juices as chyme advances from the stomach into the duodenum
- motilin, which stimulates PERISTALSIS (contractions of the gastrointestinal tract)
- gastric inhibitory polypeptide (GIP), which stimulates the pancreas to release INSULIN, slows (inhibits) the release of gastric juices, and slows stomach contractions
- enterogastrone, which stimulates the stomach to release chyme into the duodenum
- vasoactive intestinal peptide (VIP), which stops the production of gastric acid
- SOMATOSTATIN, which stops the release of insulin and further slows gastric motility (the stomach's contractions)

See also DIABETES; DIGESTIVE ENZYMES; HORMONE.

digital rectal examination (DRE) Direct palpation of the RECTUM in which the doctor inserts a gloved and lubricated finger into the rectum via the ANUS. DRE allows the doctor to feel for abnormal growths within the rectum and, in men, to palpate the PROSTATE GLAND for enlargement and possibly nodules that could suggest PROSTATE CANCER. The doctor can perform DRE as an office procedure; there is little discomfort. The person may lie on his or her side with knees drawn up. DRE may accompany a PELVIC EXAMINATION for a woman. DRE is also part of the examination to determine the cause of acute ABDOMINAL PAIN and other symptoms of health conditions affecting the lower gastrointestinal tract.

See also BENIGN PROSTATIC HYPERPLASIA (BPH); CANCER PREVENTION.

diverticular disease A chronic condition in which pockets of the gastrointestinal mucosa (inner lining of the intestines) bulge through weakened areas of the intestinal wall, forming HERNIA-like protrusions called diverticula. Diverticula may form anywhere along the gastrointestinal tract from the ESOPHAGUS to the RECTUM, though are most common in the sigmoid COLON. Most diverticular disease develops over decades and manifests symptoms after age 60. A congenital form of diverticular disease, Meckel's diverticulum, affects the SMALL INTESTINE, typically the ILEUM. Meckel's diverticulum is uncommon. Diverticulosis is the presence of multiple diverticula; diverticulitis occurs when diverticula become inflamed or infected. Doctors suspect diverticular disease results from changes in the gastrointestinal system that occur with aging. Though for some people the condition is debilitating, many people who have diverticular disease have few symp-

toms. Diverticular disease tends to have a more intense course in people who are under age 50 at the time of diagnosis.

Symptoms and Diagnostic Path

Diverticulosis often presents mild and vague symptoms such as intermittent lower abdominal discomfort or shows up incidentally on diagnostic testing for other reasons. Large or multiple diverticula may cause intestinal bleeding that may appear as darkened stools or obvious bleeding with bowel movements. Localized PAIN, especially REBOUND TENDERNESS, and FEVER suggest diverticulitis though also are symptoms of APPENDICITIS.

The diagnostic path may include DIGITAL RECTAL EXAMINATION (DRE), FECAL OCCULT BLOOD TEST (FOBT) to check for microscopic bleeding, abdominal X-ray, BARIUM ENEMA, and sigmoidoscopy or COLONOSCOPY. These procedures help distinguish between diverticulitis and appendicitis though sometimes the distinction is difficult. Diverticula often are apparent though barium enema and either sigmoidoscopy or colonoscopy provides definitive diagnosis. Occasionally the doctor may request COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to obtain detailed information on the extent of the condition or to identify a surgical emergency such as ABSCESS or PERITONITIS.

SYMPTOMS OF DIVERTICULAR DISEASE

Diverticulosis	Diverticulitis
painless rectal bleeding	pronounced and localized ABDOMINAL PAIN
	ABDOMINAL DISTENTION or rigidity
	FEVER

Treatment Options and Outlook

Diverticulitis requires treatment with ANTIBIOTIC MEDICATIONS to eradicate the INFECTION and calm the INFLAMMATION. Oral antibiotics successfully treat many people; widespread or deep infection may require intravenous antibiotics or even surgical intervention to drain the infection and remove any portions of damaged bowel. Untreated diverticulitis can result in abscess or peritonitis, which are life-threatening complications. Other complications include intestinal obstructions and fistulas (areas where the bowel erodes and establishes an opening into another structure such as the BLADDER or the VAGINA. These complications require surgical repair; a complete intestinal obstruction is an emergency.

Diverticulosis with no symptoms does not require treatment. Because diverticulosis is so prevalent among people age 50 and older, many gastroenterologists consider it nonpathologic (not a threat to health). Dietary measures such as increased fiber consumption may be enough to relieve mild symptoms such as occasional abdominal discomfort. It is important to determine the source of any intestinal bleeding, and to undergo regular COLORECTAL CANCER screening such as FOBT, sigmoidoscopy, or COLONOSCOPY. The gastroenterologist should evaluate any changes in bowel habits, persistent abdominal distention, or other circumstances that could suggest a different diagnosis.

Risk Factors and Preventive Measures

The primary risk factor for diverticulosis appears to be aging. Doctors commonly detect diverticula that do not cause symptoms in people who have gastrointestinal imaging procedures done for other reasons. People who are aware they have diverticulosis should try to maintain eating habits that support good gastrointestinal health, making sure they consume enough dietary fiber and water.

See also AGING, GASTROINTESTINAL CHANGES THAT OCCUR WITH; BOWEL MOVEMENT; GASTROINTESTINAL BLEEDING; ILEUS; PELVIC INFLAMMATORY DISEASE (PID); PROCTITIS.

duodenum The first segment of the SMALL INTESTINE, which receives partially digested and liquefied food (called chyme) from the STOMACH. The common BILE duct ends in the duodenum, channeling bile from the GALLBLADDER to the small intestine. Much of the activity of digestion takes place in the duodenum, where an abundance of DIGESTIVE ENZYMES combines with the bile to further break down food particles into their core nutrient molecules. Digestive content that leaves the duodenum for its journey through the remainder of the intestinal tract is almost watery because of the added digestive fluids. The remaining segments of the small intestine, the ILEUM and the JEJUNUM,

absorb the nutrient molecules that result from the duodenum's activity. The duodenum is the most common site of the ulcers that characterize PEPTIC ULCER DISEASE.

For further discussion of the duodenum and the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also BILE DUCTS; LIVER; PANCREAS.

dyspepsia The clinical term for indigestion or heartburn. Most people experience dyspepsia as a burning PAIN in the upper abdomen. Some people also experience NAUSEA, VOMITING, and excessive belching. Certain foods or drinks, such as spicy foods or caffeinated beverages, often worsen the discomfort, as do medications such as aspirin and other NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and numerous prescription medications. ANTACIDS sometimes bring temporary relief. PEPTIC ULCER DISEASE and GASTROESOPHAGEAL REFLUX DISORDER (GERD) are common causes of dyspepsia. Rarely, persistent dyspepsia indicates STOMACH CANCER.

The diagnostic path may include upper endoscopy, esophagogastroduodenoscopy (EGD) (examination of the ESOPHAGUS, STOMACH, and DUODENUM with a lighted, flexible tube), or BARIUM SWALLOW to rule out other causes of the symptoms. Treatment targets the underlying cause and usually includes a medication to suppress gastric acid production, such as H2 ANTAGONIST (BLOCKER) MEDICATIONS or PROTON PUMP INHIBITOR (PPI) MEDICATIONS. The doctor may also prescribe an ANTIBIOTIC MEDICATIONS to eradicate *HELICOBACTER PYLORI* BACTERIA, the typical cause of gastric and duodenal ulcers, when the underlying condition is peptic ulcer disease. Most dyspepsia dramatically improves within six to eight weeks of appropriate treatment.

See also ACHALASIA; BARRETT'S ESOPHAGUS; ENDOSCOPY; GALLBLADDER DISEASE; GASTRITIS.

E

endoscopic retrograde cholangiopancreatography (ERCP) An endoscopic procedure that allows diagnostic as well as therapeutic procedures involving the DUODENUM, pancreatic duct, and common BILE duct. After administering a sedative the gastroenterologist inserts the flexible, lighted endoscope through the MOUTH, passing it down the ESOPHAGUS and through the STOMACH to the duodenum. While advancing the endoscope the gastroenterologist examines these structures. Once the endoscope is in the duodenum, the gastroenterologist inserts a catheter through the ampulla of Vater and injects contrast into the common bile duct, pancreatic duct, and right and left intrahepatic ducts. X-rays taken after the injection of radiopaque dye into the ducts can show blockages and narrowing of the ducts. Through ERCP the gastroenterologist can take tissue samples for biopsy, remove small gallstones, and perform other treatments. ERCP takes about an hour, after which the person rests in a recovery area for another two to three hours until the sedative wears off. ERCP has few risks and can help a person avoid more invasive surgery.

See also BILE DUCTS; ENDOSCOPY; PANCREAS; PANCREATITIS; SURGERY BENEFIT AND RISK ASSESSMENT.

endoscopy The collective term for minimally invasive procedures that allow the doctor to view internal organs and structures using a lighted, flexible scope inserted through a natural body opening or through a small incision. Endoscopy can be diagnostic or therapeutic. Most endoscopic procedures require preparation before the procedure, sedation during the procedure, and supervised recovery after the procedure.

The primary risks of endoscopic procedures are minimal, consisting of primarily INFECTION or bleeding that results from unintended ABRASIONS to the tissues. A very rare but serious complication of endoscopic procedures of the bowel is perforation, in which the endoscope goes through the wall of

COMMON GASTROINTESTINAL ENDOSCOPY PROCEDURES

Procedure	Description and Purpose	Preparation
anoscopy	short, rigid scope for viewing the anal canal inserted through the ANUS diagnose HEMORRHOIDS, ANAL FISSURE, anal polyps, INFECTION	bowel evacuation (LAXATIVES or ENEMA before the procedure)
colonoscopy	flexible scope with a camera for viewing the full length of the COLON inserted through the anus detect and remove INTESTINAL POLYP diagnose inflammatory or infectious conditions evaluate bleeding or possible ILEUS (intestinal obstruction) biopsy suspicious growths or tumors	multiday bowel preparation, including dietary restrictions and a potent laxative to completely clear the colon intravenous sedation and pain medication during procedure

Procedure	Description and Purpose	Preparation
esophagoscopy	flexible scope with a camera for viewing the ESOPHAGUS inserted through the mouth diagnose esophagitis, BARRETT'S ESOPHAGUS, ESOPHAGEAL ATRESIA, HIATAL HERNIA, and ESOPHAGEAL CANCER evaluate SWALLOWING DISORDERS	fasting for 6 to 12 hours before the procedure intravenous sedation and pain medication during the procedure
esophagogastroduodenoscopy (EGD)	flexible scope with a camera for viewing the esophagus, stomach, and DUODENUM inserted through the mouth diagnose esophageal conditions, PEPTIC ULCER DISEASE evaluate upper GASTROINTESTINAL BLEEDING or PAIN, swallowing difficulties, or INFLAMMATION	fasting for 6 to 12 hours before the procedure intravenous sedation and pain medication during the procedure
gastroscopy	flexible scope with a camera for viewing the stomach inserted through the mouth take tissue samples to determine whether *HELICOBACTER PYLORI* is present cauterize bleeding ulcer	fasting for 6 to 12 hours before the procedure intravenous sedation and pain medication during the procedure
laparoscopy	flexible scope with a camera for viewing the structures of the internal abdominal cavity inserted through a small incision in the abdominal wall diagnose and treat numerous conditions (PERITONITIS, HEPATIC ABSCESS, diverticular disease, CELIAC DISEASE, gallstones, GALLBLADDER DISEASE, APPENDICITIS, PELVIC INFLAMMATORY DISEASE [PID]) numerous surgical procedures (APPENDECTOMY, CHOLECYSTECTOMY, HERNIA repair)	fasting for 6 to 12 hours before the procedure possible bowel cleansing (laxatives and enema) intravenous sedation and pain medication, epidural anesthetic, or general anesthetic
sigmoidoscopy	rigid scope or flexible scope with a camera for viewing the rectum and sigmoid colon inserted through the anus diagnose inflammation, infection, rectal polyps, rectal prolapse biopsy suspicious growths evaluate lower gastrointestinal tract bleeding	bowel evacuation (laxative or enema before the procedure)

the bowel. This requires surgical repair and ANTIBIOTIC MEDICATIONS to prevent PERITONITIS. Most people return to full and regular activities the day after diagnostic endoscopy and within a few weeks after endoscopic operations.

See also ANTIBIOTIC PROPHYLAXIS; ARTHROSCOPY; BRONCHOSCOPY; CANCER PREVENTION; CYSTOSCOPY; MINIMALLY INVASIVE SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

enema The instillation of fluid into the RECTUM through the ANUS to stimulate a BOWEL MOVEMENT. An enema may relieve CONSTIPATION or be part of the preparation to cleanse the COLON for diagnostic procedures or surgery. Frequent enemas may result in dependence on them for bowel movements. Eating a diet high in fiber helps promote healthy bowel motility to prevent constipation. Doctors sometimes prescribe enemas containing hydrocortisone (a corticosteroid medication) to treat ulcerative COLITIS, a form of INFLAMMATORY BOWEL DISEASE (IBD), to deliver the medication directly to the sites of INFLAMMATION.

See also CORTICOSTEROID MEDICATIONS; LAXATIVES.

enteritis See GASTROENTERITIS.

esophageal atresia A CONGENITAL ANOMALY in which the ESOPHAGUS fails to form properly and does not connect to the STOMACH. The esophagus may stop short at any location from the back of the THROAT to the top of the stomach or may extend to the stomach but not connect. Often there is also a tracheal–esophageal fistula (opening between the TRACHEA and the esophagus) that allows excessive air to enter the stomach and can permit saliva as well as gastric secretions to enter the LUNGS. These anomalies require emergency intervention. The risk of ASPIRATION is especially serious, as fluids in the lungs can quickly lead to INFECTION and PNEUMONIA.

Treatment requires surgery, the nature and timing of which depend on where the esophagus ends. The doctor may surgically insert a feeding tube into the stomach to instill breast milk or formula for feeding, as well as a nasogastric tube into the portion of esophagus extending from the throat to suction saliva. Because the esophagus elongates as the child grows, doctors sometimes delay complete surgical reconstruction for 6 to 18 months. The feeding and suction tubes remain in place until the surgery, sometimes a series of operations over several months, is complete.

The esophagus forms very early in PREGNANCY, at about 30 gestational days. Nearly always esophageal atresia and any related anomalies show up on prenatal ULTRASOUND so both doctors and parents can make treatment decisions before the infant's birth. Esophageal atresia tends to occur as one of numerous congenital anomalies that may involve the spine, HEART, other parts of the gastrointestinal system, the kidneys, and the extremities, a constellation doctors refer to as VACTERL. Doctors often use MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN to thoroughly examine the infant for these anomalies.

See also ANAL ATRESIA; BIRTH DEFECTS; BOWEL ATRESIA; CONGENITAL HEART DISEASE; VACTERL.

esophageal cancer Malignant growths in the ESOPHAGUS. CANCER of the esophagus takes one of two forms: ADENOCARCINOMA or squamous cell CARCINOMA. Adenocarcinoma is the more common form and nearly always originates near the esophageal entry to the STOMACH. Esophageal adenocarcinoma is nearly always a progression of BARRETT'S ESOPHAGUS, a condition in which the tissue structure of the esophagus changes to resemble that of the intestines. Adenocarcinoma can develop only in this altered tissue. Squamous cell carcinoma can develop anywhere along the esophagus and is more common in people who smoke. However, smoking, particularly in combination with excessive ALCOHOL consumption, is a major risk factor for either form of esophageal cancer. People who have untreated GASTROESOPHAGEAL REFLUX DISORDER (GERD) or ACHALASIA also face increased risk, as these conditions expose the esophagus to repeated irritation and INFLAMMATION. Though five-year survival rates have increased fourfold since the 1960s, esophageal cancer remains among the most deadly cancers because it shows few symptoms until the cancer is quite advanced.

Symptoms and Diagnostic Path

The most common symptom is difficulty swallowing (dysphagia), particularly the sensation of food

getting stuck when swallowing. Other symptoms include unintentional weight loss and sensations that are a combination of pressure and DYSPEPSIA (heartburn). Unfortunately these symptoms are vague enough that many people can ignore them or perceive them as insignificant, allowing the cancer to progress undetected.

The diagnostic path may include BARIUM SWALLOW, a series of X-rays to visualize the upper gastrointestinal tract, and ENDOSCOPY, in which the gastroenterologist directly views the esophagus using a flexible, lighted scope. Endoscopy allows biopsy of suspicious tissue. Procedures to help determine how far the cancer has spread include endoscopic ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, MAGNETIC RESONANCE IMAGING (MRI), and POSITRON EMISSION TOMOGRAPHY (PET) SCAN.

Treatment Options and Outlook

The findings of the diagnostic procedures determine treatment options, which include

- Surgery to remove the cancerous portion of the esophagus and nearby tissue; this treatment is most effective when the cancer remains confined to the area of the esophagus where it originated. The surgeon then pulls the stomach up to connect it to the shortened esophagus, or uses a segment of intestine (called a graft) to construct a replacement for the removed section.
- RADIATION THERAPY to kill the cancerous cells; this treatment typically shrinks but does not eliminate the cancer, providing relief from swallowing difficulties.
- CHEMOTHERAPY attacks cancer cells throughout the body; this treatment is most effective when the cancer has spread to other locations in the body.

Treatment often combines these approaches. Each approach has significant risks and side effects. As with all cancers, early detection significantly improves the effectiveness of treatment.

Risk Factors and Preventive Measures

The key risk factors for esophageal cancer are Barrett's esophagus and a combination of smoking and excessive alcohol consumption. Preventive measures to reduce the risk factors for esophageal cancer include

- SMOKING CESSATION
- moderation in ALCOHOL consumption
- WEIGHT LOSS AND WEIGHT MANAGEMENT
- management of chronic conditions that irritate the esophagus, notably GERD
- regular esophageal endoscopy for people who have Barrett's esophagus

See also ADENOMA-TO-CARCINOMA TRANSITION; CANCER PREVENTION; CANCER RISK FACTORS; CANCER PREVENTION; CANCER TREATMENT OPTIONS AND DECISIONS; SMOKING AND HEALTH; STAGING AND GRADING OF CANCER.

esophageal spasm Nonfunctional and often painful contractions of the muscles that line the wall of the ESOPHAGUS. The main symptom of esophageal SPASM is difficult and painful swallowing. The spasms may involve only one portion of the esophagus or the entire length of the esophagus. Doctors do not know what causes esophageal spasm, though eating foods or drinking beverages that are extremely hot or extremely cold often triggers a spasm. The diagnostic path often includes manometry, a procedure that measures pressures within the esophagus. Treatment options include medications to relax smooth MUSCLE such as nitrates and calcium channel antagonist (blocker) medications. BOTULINUM THERAPY, in which botulinum toxin injected into portions of the esophagus to paralyze it, relieves symptoms in many people.

See also ESOPHAGITIS.

esophageal varices Enlarged and weakened veins in the walls of the ESOPHAGUS. Esophageal varices result from PORTAL HYPERTENSION, a condition of impaired BLOOD flow into the LIVER, and are potentially life-threatening should they rupture and HEMORRHAGE. Portal hypertension is a common complication of conditions such as CIRRHOSIS and chronic HEPATITIS that cause SCAR tissue to develop within the liver. Symptoms include GASTROINTESTINAL BLEEDING (VOMITING blood or passing blood in the stool), thirst that increased fluid consumption does not quench, lightheadedness, and mental

confusion (hepatic ENCEPHALOPATHY) resulting from toxins the damaged liver can no longer filter from the blood.

ENDOSCOPY (in which the gastroenterologist passes a lighted, flexible scope into the upper gastrointestinal tract) is the primary diagnostic procedure, allowing the gastroenterologist to see the ESOPHAGUS, STOMACH, and DUODENUM (first segment of the SMALL INTESTINE). The endoscopy reveals the swollen veins, which the gastroenterologist can ligate (band or tie off) or inject with a DRUG to clot the blood inside the VEIN. Bleeding esophageal varices require emergency treatment, nearly always endoscopic treatment to stop the bleeding. A radiologist can do an interventional procedure called TIPPS (transjugular intrahepatic portosystemic shunt) to decrease portal pressure and stop variceal bleeding. When other efforts are not successful a surgeon may place a shunt (tube that reroutes the flow of blood) to improve blood flow into the liver, relieving the pressure blood encounters when trying to enter the liver. Usually the end treatment for esophageal varices is LIVER TRANSPLANTATION.

See also HYPOTENSION; LIVER FAILURE.

esophagitis INFLAMMATION of the ESOPHAGUS. The most common cause of esophagitis is irritation from STOMACH contents that backflow into the esophagus, such as occurs with GASTROESOPHAGEAL REFLUX DISORDER (GERD) and ACHALASIA. INFECTION resulting from HERPES SIMPLEX, CYTOMEGALOVIRUS (CMV), or yeast (*Candida*) also can involve the esophagus to cause esophagitis. Symptoms include painful or difficult swallowing and DYSPEPSIA. The diagnostic path may include ENDOSCOPY to examine, biopsy, or culture the esophagus. Treatment targets the underlying cause and may include H2 ANTAGONIST (BLOCKER) MEDICATIONS or PROTON PUMP INHIBITOR MEDICATIONS to reduce the volume of gastric acid. ANTIBIOTIC MEDICATIONS or ANTIFUNGAL MEDICATIONS are necessary to treat INFECTION. Most people fully recover when the underlying condition resolves, though often esophagitis becomes chronic.

See also BARRETT'S ESOPHAGUS; GASTRITIS; GASTROENTERITIS; SWALLOWING DISORDERS.

esophagus The muscular tube that extends from the back of the THROAT to the top of the STOMACH. From 10 to 12 inches long, the esophagus carries ingested food and fluids to the stomach to begin the process of digestion. As the esophagus leaves the throat its MUSCLE tissue is primarily striated (voluntary); as the esophagus enters the stomach its muscle tissue is smooth (involuntary). Though a person can control the initiation of swallowing, the processes that propel food down the esophagus and into the stomach are involuntary.

COMMON CONDITIONS AFFECTING THE ESOPHAGUS

ACHALASIA	BARRETT'S ESOPHAGUS
DIVERTICULAR DISEASE	DYSPEPSIA
ESOPHAGEAL ATRESIA	ESOPHAGEAL CANCER
ESOPHAGEAL SPASM	ESOPHAGEAL VARICES
ESOPHAGITIS	GASTROESOPHAGEAL REFLUX DISORDER (GERD)

For further discussion of the esophagus within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also ANUS; CECUM; COLON; DUODENUM; ILEUM; JEJUNUM; RECTUM.

F

familial adenomatous polyposis (FAP) A genetic disorder in which hundreds of intestinal polyps grow in the RECTUM and COLON. FAP is an extreme risk for early-onset COLORECTAL CANCER. This autosomal dominant disorder results from a defective gene, inherited from one parent, in which there is a MUTATION of the adenomatous polyposis coli (APC) GENE. The ACP gene regulates the proteins that inhibit adenomas (abnormal growths arising from epithelial cells, the cells that form the surface layer of SKIN and membranes) in the intestinal mucosa. The mutation of the ACP gene blocks these proteins, allowing adenomas, called intestinal polyps when they occur in the colon, to flourish. In FAP polyps are generally abundant by late ADOLESCENCE, with COLORECTAL CANCER developing before age 40.

The rapid and prolific growth of FAP-associated intestinal polyps significantly favors their evolution to malignancies, manifesting primarily as colorectal adenocarcinomas though may also occur in other sections of the gastrointestinal tract, notably the DUODENUM. FAP polyps and malignancies seldom show early symptoms; family history is the most important diagnostic factor. Signs of FAP include specific dental anomalies and retinal changes that are apparent in childhood. CANCER experts recommend screening COLONOSCOPY annually beginning in early adolescence, and every three to six months when polyp growth becomes pronounced.

Colonoscopy allows the gastroenterologist to remove large intestinal polyps and polyps showing DYSPLASIA (cellular changes indicating that ADENOMA-TO-ADENOCARCINOMA TRANSITION is under way). Studies suggest some NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) may slow the growth of adenomas, reducing the number and size of the polyps. However, these medications do not alter the course of the disease, and surgery to remove the most heavily involved sections of intestine ultimately becomes the therapeutic solution.

Doctors often recommend prophylactic total bowel resection (removal of the colon and rectum) to eliminate the potential for colorectal cancer. Presently this is the only means to prevent FAP from developing into colorectal cancer. Advances in GENE THERAPY show the greatest potential for less invasive and more effective treatments in the future. Participation in clinical research studies that are evaluating investigational treatments may present other treatment opportunities.

See also ADENOMA; CANCER PREVENTION; CANCER RISK FACTORS; CELL STRUCTURE AND FUNCTION; GENETIC DISORDERS; HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC); ILEOANAL RESERVOIR; ILEOSTOMY; INHERITANCE PATTERNS.

fatty liver See STEATOHEPATITIS.

fecal impaction Hardened pieces of feces, also called stool, that lodge in the COLON or RECTUM. Fecal impaction typically occurs as a consequence of chronic CONSTIPATION or reduced bowel motility (movement of digestive waste through the colon) and is most common in people who are confined to bed for extended periods of time. Those who take narcotic PAIN medications or ANTIDIARRHEAL MEDICATIONS may also develop fecal impaction. Symptoms may include extended time without a BOWEL MOVEMENT, lower abdominal cramping or pain, and DIARRHEA from stool leaking around the impaction. DIGITAL RECTAL EXAMINATION (DRE) allows the doctor to make the diagnosis. Treatment may include manual removal of the impaction or ENEMA to soften the impaction and stimulate

bowel movements to expel it. Increased fiber in the diet, stool softeners (medications that help the stool retain fluid), increased fluid consumption, and daily physical activity such as walking when possible can help prevent constipation and fecal impaction.

See also DIET AND HEALTH; SPINAL CORD INJURY; TOXIC MEGACOLON.

fecal incontinence Loss of bowel control. Fecal incontinence occurs more frequently in young children and in elderly adults, though can occur at any age. FECAL IMPACTION, in which stool hardens in the RECTUM, is a common cause of fecal incontinence, particularly in children, as digestive waste that continues to move through the COLON forces its way around the impaction and leaks from the ANUS because the rectum has no capacity to store it. Fecal incontinence also may result from injury or damage to the nerves that provide sensation to the perineum and rectal area or that control the anal sphincter (MUSCLE that regulates the discharge of stool). Such injury may be congenital (such as may occur with SPINA BIFIDA and other congenital anomalies affecting the SPINAL CORD), the consequence of trauma to the perineal area during CHILDBIRTH (particularly EPISIOTOMY), a complication of surgery (such as to treat HEMORRHOIDS or ANAL FISSURE), or a SIDE EFFECT of RADIATION THERAPY to treat CANCER.

Though fecal incontinence is more common among those over age 70, it is not a natural consequence of aging. Treatment can improve or eliminate fecal incontinence in most circumstances. Treatment may include "retraining" the defecation response (BIOFEEDBACK), surgery to repair damaged muscle tissues or a weakened anal sphincter, or therapies to relieve INFLAMMATORY BOWEL DISEASE (IBD) and other conditions in which there is INFLAMMATION of the colon. Eating more fruits, vegetables, and whole grain products adds fiber to the diet, which improves gastrointestinal motility (the movement of digestive content through the gastrointestinal tract). Regular physical activity, such as daily walking, also improves gastrointestinal motility.

See also CONGENITAL ANOMALY; CONSTIPATION; DIARRHEA; DIVERTICULAR DISEASE; FIBER AND GASTROINTESTINAL HEALTH; RECTAL PROLAPSE.

fecal occult blood test (FOBT) A laboratory test to determine whether there is microscopic (occult) BLOOD in the stool, primarily to screen for COLORECTAL CANCER although other conditions, such as INFLAMMATORY BOWEL DISEASE (IBD) and diverticulosis, can also cause occult bleeding. Two kinds of FOBT kits are available for self-sampling at home, one that a laboratory tests and the other that shows immediate results.

For the conventional guaiac test, the person receives a kit from the doctor. The kit contains three cards onto which the person applies a small stool sample, one sample each day for three days. The cards go into a prepaid envelope for mailing to the laboratory (or may be returned to the doctor's office). The lab applies a chemical, guaiac, that reacts with heme, a component of the HEMOGLOBIN in blood. The reaction produces a blue coloration, a positive result. No color change indicates a negative result (no blood is present).

Any positive FECAL OCCULT BLOOD TEST (FOBT) result requires further medical evaluation to determine the source of the bleeding and to rule out serious conditions such as COLORECTAL CANCER.

Tests that show immediate results are available in most pharmacies and drugstores without a doctor's prescription. They contain reagent tissues that the person drops into the toilet following a BOWEL MOVEMENT (before flushing). The tissue turns blue-green if there is any heme present, indicating blood and remains colorless when no blood is present. As with the conventional test, the person tests three bowel movements over three days. The kit includes a card that the person can fill out and send to his or her doctor or keep for personal health records.

The FOBT is a good test for colorectal cancer because the intestinal polyps that are its starting points bleed easily, though the bleeding often is not apparent with visual examination of the stool. Many health conditions can cause positive results, such as ulcers, DIVERTICULAR DISEASE, HEMORRHOIDS, and ANAL FISSURE. Certain foods and other substances can cause false-positive or false-negative results with guaiac-based tests; test instructions may advise avoiding them for 48 hours before

performing the tests (seven days for aspirin and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS [NSAIDS]). Women should do FOBT when they are not menstruating.

SUBSTANCES THAT MAY ALTER FOBT RESULTS

False-Positive Results	False-Negative Results
red meat	vitamin C supplements
cruciferous vegetables	citrus fruits and juices
cantaloupe	

Health-care professionals recommend FBOT annually starting at age 45 for both men and women as a screening for colorectal cancer. Doctors also may request FBOT when they suspect conditions that can cause GASTROINTESTINAL BLEEDING and when there is ANEMIA for no apparent reason.

See also CANCER PREVENTION; COLONOSCOPY.

fiber and gastrointestinal health Fiber, the indigestible residue of plant-based foods, adds bulk to the gastrointestinal contents. This bulk helps stimulate PERISTALSIS, the rhythmic MUSCLE contractions of the intestinal wall that move gastrointestinal contents through the digestive process. In the SMALL INTESTINE where digestive juices work to break down food particles into molecules of NUTRIENTS, the consistency fiber adds to the chyme (the thick, liquid mixture the STOMACH sends to the intestines) helps keep the food in the small intestine long enough for complete digestion to take place. In the COLON, fiber helps maintain more fluid in the stool, keeping this digestive waste soft enough to pass easily from the body during a BOWEL MOVEMENT.

A number of studies suggest a diet high in fiber and low in saturated fats measurably reduces the risk for intestinal polyps as well as for COLORECTAL CANCER. Good sources of dietary fiber include fruits, vegetables, and whole grains and whole grain products. Products such as methylcellulose (Citrucel) and psyllium (Metamucil) can supplement dietary fiber. Drinking plenty of water is also important to keep the body hydrated, which reduces the amount of water the colon extracts from digestive waste.

See also CONSTIPATION; DIARRHEA; INTESTINAL POLYP; NUTRITIONAL NEEDS.

flatulence The clinical term for intestinal gas. Flatulence indicates undigested food particles are present in the COLON. Consuming large quantities of indigestible fiber (such as with beans and other legumes), eating too fast to thoroughly chew food before swallowing, and eating a larger quantity of food than the gastrointestinal tract can accommodate are common reasons for excessive amounts of undigested food particles to make it to the colon. BACTERIA naturally present in the colon act on these food particles. In addition to breaking them down into nutrient molecules, the bacteria also produce gas as a byproduct. These gases eventually make their way through the colon and escape through the ANUS. The most common of these are methane and hydrogen sulfide, which give flatulence its characteristic odor. Excessive flatulence often causes lower abdominal discomfort and cramping. It may occur with LACTOSE INTOLERANCE, CARBOHYDRATE INTOLERANCE, and MALABSORPTION and as a SIDE EFFECT of numerous medications. The herbs peppermint, GINGER, and CHAMOMILE reduce intestinal gas, as do products containing simethicone, activated charcoal, or enzymes that help break down cellulose (residual fiber).

See also ANTACIDS.

G

gallbladder A small, muscular pouch on the underside of the LIVER that concentrates and stores BILE. The gallbladder absorbs about 90 percent of the water in the bile that arrives from the liver, creating concentrated, potent bile. Fats and proteins in the chyme (partly digested food) the STOMACH sends to the DUODENUM trigger the duodenum to release the digestive HORMONE cholecystokinin (CCK). CCK stimulates the gallbladder to contract, expelling bile into the duodenum to aid with digestion. The most common health conditions that affect the gallbladder are cholelithiasis (gallstones), cholecystitis (INFLAMMATION of the gallbladder), and biliary dyskinesia (inadequate contraction of the gallbladder). CANCER of the gallbladder occurs though is rare.

For further discussion of the gallbladder within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also CHOLECYSTECTOMY; DIGESTIVE HORMONES; GALLBLADDER DISEASE.

gallbladder disease Disorders and dysfunctions of the GALLBLADDER. Gallbladder disease becomes more common with increasing age. Though medical treatments can help some people with gallbladder disease, surgery to remove the gallbladder is the most common treatment and permanently resolves symptoms in about 90 percent of people who have primary gallbladder disease. Tumors and CANCER of the gallbladder occur, though are very rare. INFLAMMATION of the BILE DUCTS and HEPATITIS also can affect BILE production and gallbladder function. Gallbladder disease can be acute or chronic.

Biliary dyskinesia Dysfunction of the gallbladder prevents it from contracting to eject bile, reducing or stopping the flow of bile from the gallbladder to the DUODENUM (first segment of the small intestine). Biliary dyskinesia may occur as a result of injury to the nerves that supply the gallbladder, as a consequence of metabolic disorders affecting LIVER function, or for unknown reasons (most common).

Cholelithiasis Commonly called gallstones, cholelithiasis develops over years to decades in most people. Gallstones can range in size from a few millimeters to several centimeters. There can be one to a few to dozens. About 80 percent of gallstones contain mostly cholesterol; bile pigments such as BILIRUBIN make up the remainder. Many people have gallstones without symptoms. Gallstones become a health concern when they lodge in the bile ducts or when they cause irritation and inflammation of the gallbladder's mucosal lining. In a variation of cholelithiasis, called choledocholithiasis, the gallstones form in the bile ducts.

Cholecystitis Inflammation or INFECTION of the gallbladder most commonly occurs in conjunction with gallstones that block the flow of bile out of the gallbladder, though it can develop in biliary dyskinesia when the bile in the gallbladder stagnates. This stagnation irritates and inflames the lining of the gallbladder. Cholecystitis that occurs without gallstones is acalculus cholecystitis.

GALLBLADDER DISEASE AND WEIGHT LOSS

These weight-loss efforts increase the risk for gallbladder disease:

- rapid weight loss (3 pounds a week or greater)
- BARIATRIC SURGERY (gastric banding, stapling, bypass)
- weight loss cycling (cycles of loss and regaining weight, especially large amounts)

Symptoms and Diagnostic Path

PAIN is the primary symptom of gallbladder disease, and is characteristically:

- steady, sometimes intense pain between the right rib cage and shoulder blade felt in the front, back, or both
- brought on by eating fatty foods, often occurring several hours after eating
- common at night, waking one from sleep
- one to five hours in duration
- not relieved by changing positions or taking over-the-counter pain medications

Other symptoms of gallbladder disease include NAUSEA, VOMITING, gastrointestinal distress (gas, bloating, DIARRHEA) not relieved by ANTACIDS, and light-colored stools that contain noticeable mucus. When a gallstone blocks a bile duct there often is JAUNDICE (yellowish discoloration of the SKIN) and severe tenderness over the site of the blockage. FEVER, chills, and unrelenting pain may signal an infection in the gallbladder. These circumstances require immediate medical attention.

The doctor's physical examination includes a careful history of symptoms as well as palpation of the abdomen. The diagnostic path typically includes ULTRASOUND of the upper right abdomen, which can detect gallstones as small as 2 millimeters—about the size of a thick pencil lead. It also can show thickening of the gallbladder's wall, an indication of chronic inflammation and previous gallstone development. Because the liver shadows the gallbladder, ultrasound does not always detect inflammation related to acute cholecystitis or certain other gallbladder problems. Contrast dye X-RAY (oral or intravenous) and radioisotope imaging (cholescintigraphy) provide detailed information about gallbladder function.

Treatment Options and Outlook

Mild and infrequent symptoms may require no intervention beyond watchful waiting and lifestyle modifications such as eating a diet lower in fat, getting daily physical exercise, and WEIGHT LOSS AND WEIGHT MANAGEMENT. ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) often is successful in removing small gallstones from the bile ducts.

Surgery to remove the gallbladder (CHOLECYSTECTOMY) is the treatment of choice for acute, recurrent, or chronic cholecystitis and cholelithiasis in which gallstones cause pain and bile duct obstruction. There are two methods for performing cholecystectomy: laparoscopic surgery and OPEN SURGERY. About 95 percent of cholecystectomies performed in the United States are laparoscopic.

Medications to dissolve gallstones are not very successful and can cause significant side effects. Current treatment guidelines recommend these medications only when surgery is not a viable option. The two drugs doctors sometimes use are ursodiol (Actigall) and chenodiol (Chenix). Though EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY (ESWL) is effective in breaking up KIDNEY stones, it so far has not proven to be successful in doing the same with gallstones.

About a third of people who have one gallbladder episode, such as a gallstone that causes pain, never have another. The gallbladder is an organ that, though useful, the body does not require. Most people make a full recovery from gallbladder surgery and can resume their normal activities without modification. No dietary restrictions or medications are necessary.

Risk Factors and Preventive Measures

Women are twice as likely as men to develop gallbladder disease. Researchers believe this increased risk correlates to the presence of ESTROGENS, which play an integral role in cholesterol METABOLISM. Women who are pregnant or taking oral contraceptives (birth control pills), which increase the body's level of estrogen, are at highest risk. Gallbladder disease seldom occurs in children.

These factors increase the risk for gallbladder disease in men and women alike:

- OBESITY
- rapid weight loss or weight cycling
- DIABETES
- taking lipid-lowering medications
- age 60 or older

Lifestyle habits such as nutritious diet and regular physical exercise minimize the likelihood of

gallbladder disease. Dietary fiber helps absorb cholesterol from consumed foods, reducing the amount of cholesterol that becomes available in the bloodstream and for the liver to process.

See also DIET AND HEALTH; ENDOSCOPY; HYPERLIPIDEMIA; LIFESTYLE AND HEALTH; MINIMALLY INVASIVE SURGERY; PRIMARY BILIARY CIRRHOSIS; PRIMARY SCLEROSING CHOLANGITIS.

gastrectomy Partial or complete surgical removal of the STOMACH, typically to treat STOMACH CANCER or uncontrollable bleeding resulting from PEPTIC ULCER DISEASE. Gastrectomy is a major OPERATION, typically an OPEN SURGERY, performed under general ANESTHESIA that requires several days to a week in the hospital and 8 to 12 weeks for total recovery and return to regular activities. An individual's course of recovery depends on the reasons for the surgery. The surgical operation takes two to three hours. After removing the diseased portion of the stomach through an abdominal incision at the lower edge of the left rib cage, the surgeon connects the remaining portion of the stomach (or the ESOPHAGUS, when the gastrectomy is total) to the DUODENUM. A partial (also called subtotal) gastrectomy leaves a gastric pouch that can carry on some of the digestive functions of the stomach. Total gastrectomy, which is less common, leaves no residual gastric pouch though the surgeon may construct one by expanding a portion of the duodenum.

Many people are able to return to normal eating habits after they recover from the surgery, though find that they need to eat frequent small meals to accommodate the smaller stomach and reduce gastrointestinal distress. Foods that are high in protein and low in simple sugars are easier for the small intestine to digest without the aid of the stomach. Some people have difficulty eating regular foods after gastrectomy and need to use NUTRITIONAL SUPPLEMENTS, typically liquid preparations, to meet their NUTRITIONAL NEEDS.

Risks and complications of gastrectomy include bleeding, INFECTION, dumping syndrome (RAPID GASTRIC EMPTYING), and damage to the vagus NERVE (which regulates gastric PERISTALSIS and other digestive functions). People who have total gastrectomies, and many people who have subtotal gastrectomies, need regular injections of vitamin B_{12} (cyanocobalamin) because the gastric mucosa is no longer able to produce intrinsic factor, a chemical substance that allows the SMALL INTESTINE to absorb this vital nutrient. Vitamin B_{12} deficiency causes pernicious ANEMIA.

See also BARIATRIC SURGERY; CANCER TREATMENT OPTIONS AND DECISIONS; CRANIAL NERVES; SURGERY BENEFIT AND RISK ASSESSMENT.

gastritis INFLAMMATION of the lining of the STOMACH. There are two broad classifications of gastritis: erosive and nonerosive. The most common cause of erosive gastritis is repeated irritation from ingested substances such as ALCOHOL, aspirin, and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). The most common cause of nonerosive gastritis is INFECTION with *HELICOBACTER PYLORI*, the strain of BACTERIA that causes PEPTIC ULCER DISEASE. Occasionally viral infections can cause acute gastritis, which resolves when the infection runs its course. Autoimmune gastritis, in which the IMMUNE SYSTEM attacks the cells that form the mucosal lining of the stomach, interferes with the absorption of certain NUTRIENTS, notably vitamin B_{12} (pernicious ANEMIA).

Symptoms include DYSPEPSIA (upset stomach), PAIN, NAUSEA, VOMITING, and a sensation of fullness. The diagnostic path may include BARIUM SWALLOW and endoscopic examination of the ESOPHAGUS, stomach, and DUODENUM (first segment of the SMALL INTESTINE and the site of peptic ulcer disease). The gastroenterologist may biopsy samples of stomach tissue. Treatment targets the underlying cause. Eliminating ingestion of the responsible substance often ends erosive gastritis. ANTIBIOTIC MEDICATIONS can eradicate *H. pylori*. Treatment for autoimmune gastritis focuses on countering any NUTRITIONAL DEFICIENCY that results as well as eliminating other sources of irritation to minimize gastric inflammation.

See also AUTOIMMUNE DISORDERS; COLITIS; ENDOSCOPY; GASTROENTERITIS; PANCREATITIS; STOMACH CANCER.

gastroenteritis INFLAMMATION of the SMALL INTESTINE. The most common cause of gastroenteritis is viral INFECTION, though sometimes BACTERIA or PARASITES are responsible. The inflammation of the intestinal mucosa (mucus lining of the intestinal

wall) reduces the small intestine's ability to absorb NUTRIENTS and fluid. People often refer to gastroenteritis as "stomach flu," though this is inaccurate; the "flu" or influenza is a viral infection of the pulmonary system.

Symptoms and Diagnostic Path

Symptoms of gastroenteritis include DIARRHEA, abdominal cramping, and occasionally ABDOMINAL DISTENTION. Depending on the cause of the infection, the diarrhea can be profuse or bloody; bloody diarrhea requires medical evaluation. There may also be FEVER and VOMITING.

Symptoms that extend beyond two or three days in children or the elderly, or in a person of any age who cannot keep any fluids down, require medical evaluation to prevent DEHYDRATION.

The diagnostic path may include laboratory tests to determine the presence of pathogens (agents of infection) in the stool and blood tests to help identify the extent and nature of infection. The doctor may take stool samples or a rectal swab to determine whether bacterial or parasitic pathogens are present, which would require treatment with the appropriate medications. Bacterial gastroenteritis most often results from consuming contaminated food or water. The doctor may recommend ANTIEMETIC MEDICATIONS to quell nausea and ANTIDIARRHEAL MEDICATIONS to reduce diarrhea, depending on the cause and extent of the symptoms.

Noninfectious forms of gastroenteritis include Crohn's disease and radiation gastroenteritis. Crohn's disease is a component of INFLAMMATORY BOWEL DISEASE (IBD), which many doctors believe is an autoimmune disorder with a genetic component in which the IMMUNE SYSTEM attacks the intestinal mucosa. The attacks result in small ulcerations that often bleed. The enteric symptoms are chronic; treatment targets the underlying disease. Radiation gastroenteritis results from damage to the intestinal mucosa that occurs with RADIATION THERAPY to the abdomen, and may be acute (limited to the course of radiation therapy) or chronic (signaling permanent changes in the intestinal mucosa).

COMMON ENTERIC PATHOGENS

Pathogen	Type	Route of Infection
astrovirus	VIRUS	contaminated food or water person-to-person
calicivirus	virus	contaminated food or water person-to-person
Cryptosporidium	PARASITE	contaminated water animal-to-person person-to-person
Cyclospora cayetanensis	parasite	contaminated food or water person-to-person
enteric adenovirus	virus	contaminated food or water person-to-person
Escherichia coli	BACTERIA	contaminated food or water person-to-person
Giardia lamblia	parasite	contaminated water person-to-person
Listeria	bacteria	contaminated food person-to-person
Microsporidia	parasite	unknown
rotavirus	virus	contaminated food or water person-to-person
Salmonella	bacteria	contaminated food reptile-to-person
Staphylococcus enterotoxin	bacteria	contaminated food person-to-person

Treatment Options and Outlook

Adequate fluid replacement and other supportive measures are the only treatment necessary for viral gastroenteritis, which typically runs its course in three to five days. Young children, older adults, and people who have serious chronic health care conditions are at greatest risk for complications from viral gastroenteritis, though most people recover fully. Bacterial and parasitic gastroenteritis require treatment with the appropriate medications to eliminate the causative PATHOGEN,

and sometimes have a longer course of illness than viral gastroenteritis. Treatment for radiation gastroenteritis focuses on dietary management (eating frequent small meals and foods high in fiber) with ANTIDIARRHEAL MEDICATIONS to help control diarrhea.

Risk Factors and Preventive Measures

Viral gastroenteritis is highly contagious and often occurs in outbreaks, particularly in group settings such as schools, day cares, nursing homes, camps, and contained environments such as cruise ships. These methods can significantly reduce infectious gastroenteritis:

- proper food handling and preparation
- frequent and thorough HAND WASHING
- drinking WATER PURIFICATION (boiling, filtration, chemical)

See also AMEBIASIS; COLITIS; CYCLOSPORIASIS; FOODBORNE ILLNESSES; FOOD SAFETY; GASTRITIS; GIARDIASIS; LISTERIOSIS; PARASITE; SALMONELLOSIS; SHIGELLOSIS; WHIPPLE'S DISEASE.

gastroesophageal reflux disorder (GERD) A chronic condition in which gastric contents leak back from the STOMACH into the ESOPHAGUS. Because stomach juices are highly acidic, this backwash creates chemical BURNS in the delicate tissues of the esophagus. The lining of the esophagus lacks the protective mucus that safeguards the stomach from gastric acid, making it vulnerable to injury. Up to 40 percent of adults in the United States have GERD. Though GERD can develop in people of any age, including children, the likelihood of it doing so increases with age. Treatments to manage GERD include medical, surgical, and lifestyle methods.

Symptoms and Diagnostic Path

The symptoms of GERD often appear or are more severe following meals, when lying on the back, when bending over, and when lifting or straining. Many people experience more severe symptoms at night that awaken them from sleep. Typical GERD symptoms are chronic (ongoing) and include

- PAIN, pressure, or burning sensation in the mid-chest
- NAUSEA, and less commonly VOMITING, after eating
- regurgitation (reflux) of stomach contents up to several hours after eating that causes a bitter taste in the MOUTH and a burning sensation in the THROAT
- a sense of fullness in the stomach even when hungry

Some people also experience chronic sore throat or hoarseness resulting from the persistent reflux, or HICCUPS, likely due to irritation of the DIAPHRAGM, where the esophagus and stomach join, which is the site of the irritation. The diagnostic path may include BARIUM SWALLOW, gastroesophagoscopy (endoscopic examination of the esophagus and stomach), and breath or BLOOD tests for the presence of *HELICOBACTER PYLORI*. Because GERD is so common and the diagnostic procedures are invasive, doctors often use a trial of medication, such as H2 ANTAGONIST (BLOCKER) MEDICATIONS or PROTON PUMP INHIBITOR MEDICATIONS (PPIs), to suppress gastric acid production and then assume a diagnosis of GERD if the medication relieves the symptoms.

Treatment and Outlook

Most people obtain full relief from their symptoms with a combination of medical treatments and lifestyle modifications. Many people find lifestyle modifications (diet, WEIGHT LOSS AND WEIGHT MANAGEMENT, SMOKING CESSATION) combined with ANTACIDS adequate, while other people require stronger medications such as H2 blockers or PPIs. Many H2 blockers are available in over-the-counter formulas. Reducing gastric acid significantly reduces the amount reflux that can backwash into the esophagus.

The most common surgical treatment for GERD that fails to improve with medication and lifestyle methods, fundoplication, reinforces the upper section of the stomach (the fundus) to increase tension on the lower esophageal sphincter. There are several fundoplication methods, some of which the surgeon can perform laparoscopically and others that require OPEN SURGERY. Another surgical option is endoscopic gastroplasty to repair or strengthen the lower esophageal sphincter. The

TREATMENTS FOR GERD

Medical Methods	Surgical Methods	Lifestyle Methods
H2 BLOCKERS	fundoplication	WEIGHT LOSS AND WEIGHT MANAGEMENT
PPIs	endoscopic gastroplasty	elevate head of bed
antibiotics for *H. PYLORI*		SMOKING CESSATION
ANTACIDS		avoid CAFFEINE and ALCOHOL
		reduce carbonated beverages
		stay upright for 2 hours after meals
		sleep lying on the left side
		avoid NSAIDs and aspirin

most common complications after surgery are INFECTION and difficulty swallowing.

Risk Factors and Preventive Measures

Doctors are uncertain what causes GERD to develop, though various factors appear to contribute. Among them are

- OBESITY
- cigarette smoking
- *H. pylori*
- ASTHMA
- eating within two hours of going to bed
- heavy ALCOHOL consumption

Preventive measures include avoiding or minimizing factors associated with GERD as well as eating smaller meals and getting regular physical exercise, which helps maintain effective PERISTALSIS and gastrointestinal motility (movement of food through the gastrointestinal tract).

See also ACHALASIA; BARRETT'S ESOPHAGUS; ENDOSCOPY; ESOPHAGITIS.

gastrointestinal bleeding Gross (obvious) or occult (microscopic) bleeding along any section of the gastrointestinal tract. Gross bleeding generally is obvious. Occult bleeding often occurs with intestinal polyps. FECAL OCCULT BLOOD TEST (FOBT) is one method used to detect microscopic BLOOD in the stool. Several kinds of FOBTs are available for home use, though it is imperative to follow up with the doctor when the results are questionable or positive.

Gastrointestinal bleeding can result from numerous conditions as well as excessive doses of anticoagulant medications or irritation from medications such as aspirin and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). The most common sites are the STOMACH, DUODENUM, sigmoid COLON, and RECTUM. There are three ways in which gastrointestinal bleeding presents:

- hematemesis is the VOMITING of bright red blood, signaling bleeding from the upper gastrointestinal tract (usually the ESOPHAGUS, stomach or duodenum)
- hematochezia is the passing of bright red blood rectally, indicating bleeding from the lower gastrointestinal tract (usually the sigmoid colon or rectum) or from HEMORRHOIDS
- melena is the passing of dark, tarry stools that signal bleeding from the upper gastrointestinal tract

All gastrointestinal bleeding requires medical evaluation to determine its cause. Persistent bleeding, even when the amounts of blood appear small, results in ANEMIA. The diagnostic path may include ENDOSCOPY of the upper and lower gastrointestinal tracts, esophagogastroduodenoscopy (EGD) and COLONOSCOPY respectively, as well as BARIUM SWALLOW and BARIUM ENEMA. Treatment targets the underlying condition, and may include BLOOD TRANSFUSION when the blood loss is significant.

CONDITIONS THAT CAN CAUSE GASTROINTESTINAL BLEEDING

ANAL FISSURE	BARRETT'S ESOPHAGUS
COLITIS	DIVERTICULAR DISEASE
ESOPHAGEAL CANCER	GASTRITIS
HEMORRHOIDS	INFLAMMATORY BOWEL DISEASE (IBD)
INTESTINAL POLYP	PEPTIC ULCER DISEASE
STOMACH CANCER	

See also ESOPHAGEAL VARICES; HEMORRHAGE.

gastroparesis Slowed function of the STOMACH that delays the travel of gastric contents into the DUODENUM. Gastroparesis results from disturbances of or damage to the vagus NERVE (the tenth cranial nerve), which carries the nerve impulses that accelerate PERISTALSIS (rhythmic contractions of the gastrointestinal tract). Gastroparesis most commonly occurs after a viral infection though also is a complication of DIABETES, which damages nerve structures throughout the body. Other causes include sclerotic conditions such as MULTIPLE SCLEROSIS or scleroderma, anticholinergic medications often prescribed to treat PARKINSON'S DISEASE, inadvertent damage to the vagus nerve as a complication of thoracic or HEART surgery, and intentional interruption of the vagus nerve (vagotomy) to treat conditions such as PEPTIC ULCER DISEASE. People who are on long-term PARENTERAL NUTRITION also often have gastroparesis.

The main symptom of gastroparesis is frequent VOMITING of undigested food hours after a meal. Other symptoms may include lack of APPETITE due to sense of fullness, NAUSEA, ABDOMINAL DISTENTION, and unintended weight loss. Gastroparesis can quickly result in DEHYDRATION, which can create significant disturbances of blood GLUCOSE and INSULIN levels in people who have diabetes. The first approach of treatment is to shift to eating numerous small meals throughout the day, attempting to slow the pace of ingestion to accommodate the stomach's slowed functioning.

Medications to stimulate gastrointestinal motility, such as metoclopramide (Reglan), may improve gastric emptying. Control of diabetes, which may require multiple insulin doses throughout the day, is crucial. If symptoms continue, the gastroenterologist may suggest a jejunostomy tube, or feeding tube, that bypasses the stomach. Most people, however, achieve an acceptable resolution of their symptoms, even when gastroparesis persists, through nonsurgical approaches.

See also CRANIAL NERVES; ENTERAL NUTRITION; NUTRITIONAL NEEDS; PANCREATITIS; RAPID GASTRIC EMPTYING.

H

heartburn See DYSPEPSIA.

Helicobacter pylori The BACTERIA responsible for much PEPTIC ULCER DISEASE and STOMACH CANCER. Researchers isolated *H. pylori* in 1982, a discovery that dramatically altered the treatment approach to ulcers. Though researchers do not know how *H. pylori* enter the gastrointestinal system, they believe INFECTION occurs early in life in most people. The bacteria establish themselves in the lining of the STOMACH in the area called the pylorus, and often in the DUODENUM (first segment of the SMALL INTESTINE) as well. The presence of *H. pylori* causes irritation, which the body counters with an inflammatory response in an attempt to buffer the gastric mucosa from the irritation. Over time this pattern of irritation and INFLAMMATION results in ulcerative erosions of the mucosa, commonly called stomach ulcers.

The urea breath test is a simple, accurate, and fast way for doctors to determine whether *H. pylori* are present. The person drinks a solution or swallows a capsule containing urea tagged with a carbon isotope. *H. pylori* metabolize the urea, releasing carbon dioxide containing the carbon isotope. A machine analyzes breath samples to detect the presence of carbon isotopes in the carbon dioxide. Endoscopic biopsy, blood tests to detect *H. pylori* antibodies, and stool tests that detect *H. pylori* antigens are other methods to diagnose *H. pylori* infection. As well, these tests show whether treatment with ANTIBIOTIC MEDICATIONS has successfully eradicated the bacteria.

H. pylori are sensitive to several antibiotics though have the ability to rapidly adapt and develop resistance. For this reason doctors prescribe two kinds of antibiotic medications in combination. Treatment also includes PROTON PUMP INHIBITOR (PPI) MEDICATIONS or H2 ANTAGONIST (BLOCKER) MEDICATIONS to suppress gastric acid production, which makes the stomach a more hostile environment for the *H. pylori* and reduces irritation to the inflamed tissues or ulcers. *H. pylori* are also sensitive to the common ANTIDIARRHEAL MEDICATION bismuth subsalicylate (Pepto-Bismol). There are numerous treatment protocols for eradicating *H. pylori* that use these medications in various combinations. Once eradicated, *H. pylori* seem not to recur.

See also ANTIBODY; ANTIGEN; CANCER RISK FACTORS; ENDOSCOPY; GASTRITIS.

hemorrhoids Veins and related structures in and around the ANUS that distend and swell. Hemorrhoids can be internal or external. An old term for hemorrhoids that remains in common use is piles, a reference to the appearance of external hemorrhoids. Hemorrhoids alone do not cause symptoms; about two thirds of adults in the United States have hemorrhoids. Hemorrhoids cause PAIN, itching, and bleeding when they become inflamed, develop BLOOD clots, or prolapse (protrude). Factors that contribute to symptomatic hemorrhoids include

- chronic CONSTIPATION and straining with BOWEL MOVEMENTS
- sitting on the toilet for extended periods of time, which reduces blood circulation
- low fiber diet, which results in small, hard stools that can be difficult to pass
- PREGNANCY, which pressures the pelvic floor and can affect perineal blood flow
- INFLAMMATORY BOWEL DISEASE (IBD)

The doctor can diagnose hemorrhoids via physical examination of the anal area, including DIGITAL RECTAL EXAMINATION (DRE) or anoscopy, when symptoms are mild. Treatment attempts to shrink and soothe the irritated tissues. Topical preparations containing an anesthetic agent and hydrocortisone can provide prompt, short-term relief. A SITZ BATH, or simply soaking in the bathtub, relaxes the anal sphincter enough to calm the spasms that prolapsed or thrombosed (clotted) hemorrhoids cause. Dietary changes (such as increased fiber and fluids) combined with frequent physical activity (such as walking) help to reduce constipation, which relieves straining and pressure on the anorectal area. The doctor can ligate (band off), cauterize, freeze, or excise (cut out) hemorrhoids that fail to respond to conservative treatment approaches. In the vast majority of people, appropriate treatment and lifestyle modifications end symptoms.

See also ANAL FISSURE; ENDOSCOPY.

hepatic abscess A pocket of INFECTION that develops within the LIVER, also called liver ABSCESS. Though not common, hepatic abscesses can develop as a complication of GALLBLADDER DISEASE in which infection spreads through the BILE DUCTS to the liver. Symptoms include ABDOMINAL PAIN (often focused in the upper left quadrant), tenderness and rigidity, and FEVER. A person with a hepatic abscess often appears very ill. Abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI) are among the diagnostic procedures that help detect hepatic abscess. Treatment is percutaneous aspiration (inserting a needle through the SKIN and into the abscess) or laparoscopic surgery to drain the collected pus, with intensive antibiotic therapy to eradicate the infection. An untreated hepatic abscess can quickly become life-threatening, as the liver's rich blood supply can carry the pathogenic bacteria throughout the body.

See also ANTIBIOTIC MEDICATIONS; MINIMALLY INVASIVE SURGERY; SEPTICEMIA.

hepatic cyst A noncancerous growth, often fluid-filled, that develops in the LIVER. Most simple hepatic cysts cause no symptoms; they become apparent during diagnostic procedures, such as abdominal ULTRASOUND, done for other reasons. When there are no symptoms, no treatment is necessary beyond regular monitoring (watchful waiting). A hydatid cyst contains the larvae of the PARASITE *Echinococcus granulosus,* acquired through contact with animal feces that contain the parasite's eggs, which migrate to the liver. A hydatid cyst grows slowly though can become large enough to hold a liter or more of fluid. Even when hydatid cysts show no symptoms, doctors remove them because they can cause life-threatening complications such as PERITONITIS or SEPTICEMIA if they rupture. Removal of a hepatic cyst is nearly always a laparoscopic surgery.

See also MINIMALLY INVASIVE SURGERY; PERCUTANEOUS LIVER BIOPSY.

hepatitis INFLAMMATION of the LIVER. There are numerous kinds and causes of hepatitis. Most hepatitis results from specific viruses that cause infections of the liver, ALCOHOL abuse, and hepatotoxic drugs. Hepatitis is the leading cause of LIVER FAILURE, and reason for LIVER TRANSPLANTATION, in the United States.

Infectious (viral) hepatitis The viruses that cause viral hepatitis belong to several virus families: the picornavirus family, which causes hepatitis A; the hepacivirus family, which causes hepatitis B; and the flavirus family, which causes hepatitis C.

Though these viruses are among the smallest researchers have yet detected, they cause a wide range of illnesses from COLDS to viral MENINGITIS to POLIO. Researchers refer to those that specifically target the liver as hepatotropic and label them alphabetically in the sequence of their discovery. Each individual VIRUS has unique characteristics that cause a particular pattern of disease. Researchers classify viral hepatitis according to the viral variant responsible for the disease response.

Five viruses identified as hepatotropic ("liver loving") cause 95 percent of the infectious hepatitis diagnosed in the United States: hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis D (HDV), and hepatitis E (HEV). Hepatitis A and hepatitis E cause acute infection only and rarely cause permanent liver damage, though hepatitis A infection can cause serious illness and fatality. Hepatitis A accounts for more than 60

percent of hepatitis cases in the United States and hepatitis B for nearly 30 percent. Other identified hepatitis viruses (HFV and HGV) are rare in the United States. Hepatitis B and hepatitis C can be present without showing symptoms; about a third of people who have hepatitis B are carriers (the virus is present in their bodies and infects others, though does not cause illness in them). Though health agencies routinely test donated BLOOD, tissue, and organs for hepatitis (as well as numerous other infectious agents), people who receive donor substances face some risk of infection. Hepatitis C accounts for about 80 percent of such infections; new infections have become rare as a result of stringent donor substances screening. Hepatitis D can replicate only when hepatitis B is also present. It often causes "superinfection"—acute disease with chronic hepatitis B infection. Hepatitis E occurs in outbreaks related to water contamination, such as might follow widespread flooding, and tend to be more common among people who contract the virus during travel to developing countries where COMMUNITY SANITATION is inadequate.

Viral hepatitis begins with an acute illness that lasts from 2 to 10 months, though in most people the acute phase resolves in 4 to 6 months. Chronic forms of hepatitis often follow infection with HBV and HCV, resulting in recurring episodes of symptoms. The repeated inflammation is very harmful to the liver, causing scarring (fibrosis) that eventually becomes CIRRHOSIS (SCAR tissue replaces liver tissue). The damage tends to be progressive, culminating in liver failure in about 25 percent of

Hepatitis Virus	Mode of Infection	Preventive Measures
hepatitis A (HAV)	fecal-oral food-borne person-to-person occupational exposure	vaccination frequent HAND WASHING and conscientious PERSONAL HYGIENE postexposure prophylaxis
hepatitis B (HBV)	blood sexual contact shared needles among illicit injected DRUG users perinatal (to infant at birth) hemodialysis occupational exposure	vaccination safer sex practices avoid sharing needles barrier precautions to prevent occupational exposure postexposure prophylaxis
hepatitis C (HCV)	blood sexual contact shared needles among illicit injected drug users perinatal (to infant at birth) hemodialysis occupational exposure	safer sex practices avoid sharing needles barrier precautions to prevent occupational exposure postexposure prophylaxis
hepatitis D (HDV)	blood shared needles among illicit injected drug users occupational exposure	HBV vaccination (HDV can infect people only already infected with HBV) avoid sharing needles barrier precautions to prevent occupational exposure postexposure prophylaxis
hepatitis E (HEV)	fecal-oral water	boiling water when contamination is possible

people who have chronic hepatitis. About 10 percent of people who develop chronic hepatitis subsequently develop LIVER CANCER. People who have chronic forms of hepatitis may show no signs or symptoms of disease though are carriers who pass the virus to others with whom they have close contact (particularly sexual contact).

Alcoholic hepatitis Alcohol is highly toxic to the liver. Chronic alcohol abuse results in repeated inflammation of liver tissue, with resulting scarring (fibrosis) that ultimately limits the liver's ability to function (cirrhosis). Liver damage that occurs is permanent and may lead to liver failure.

Hepatotoxic hepatitis The most common hepatotoxins resulting in hepatitis are acetaminophen (Tylenol) and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen (Motrin). Other hepatotoxins include cleaning solutions, industrial pollutants, and carbon tetrachloride. Hepatotoxic hepatitis can result in rapid liver failure or lead to chronic hepatitis.

Symptoms and Diagnostic Path

The general symptoms of hepatitis are the same regardless of the cause and occur in four distinct stages:

1. Infective asymptomatic, in which the virus has invaded the liver and is replicating. During this stage the person is most highly infective.
2. Prodromal, in which infection has not yet manifested symptoms but the person begins to feel generalized malaise, loss of APPETITE, and aversions to certain foods (and often to cigarette smoke).
3. Active disease response, with characteristic symptoms that include JAUNDICE, dark urine, pale stools, FEVER, fatigue, and abdominal tenderness.
4. Recovery, during which the person continues to feel fatigue and malaise but liver functions are returning to normal, or liver failure, indicating the disease process has overwhelmed the liver.

Viral hepatitis remains infectious for as long as the virus is active in the body. With chronic forms of viral hepatitis, symptoms recur periodically. Alcoholic hepatitis and hepatotoxic hepatitis remain in active disease state until the causative substance clears the body.

Treatment Options and Outlook

Treatment for hepatitis is largely supportive, consisting of fluid consumption, adequate nutrition, and rest. The course of acute disease may be mild and flulike or life-threatening, depending on numerous variables such as the cause and the individual's personal health status. People who have IMMUNE SYSTEM impairments, such as those who have HIV/AIDS, are very young, or are very old are at greatest risk for severe disease. ANTIVIRAL MEDICATIONS such as adefovir, ribavirin, interferon, amantadine, and lamivudine sometimes limit the course of active disease in chronic hepatitis (HBV and HDV). Liver damage due to hepatotoxic hepatitis may so overwhelming as to require immediate liver transplantation.

Chronic hepatitis remains a significant lifelong threat to health. Those who have chronic infectious hepatitis can pass the disease to others. Regardless of cause, chronic hepatitis limits the liver's ability to function. Physiologic stress, such as alcohol consumption or taking certain medications, can seriously strain the liver's capacity. People who have chronic hepatitis may experience frequent bouts of fatigue. Many people are able to enjoy relatively normal lifestyles, though must remain mindful of situations and substances that could challenge the liver.

Risk Factors and Preventive Measures

The primary risk factor for infectious hepatitis is exposure to others who have hepatitis infections. For hepatitis A, this includes consuming foods handled in an unsafe manner by a person who already has hepatitis A infection or handling contaminated fecal waste (such as diapers). Those at risk for blood-borne hepatitis infections (HBV, HCV, HDV) include

- people who have unprotected sex with multiple partners (hepatitis B is especially common among men who have sex with men)
- people who inject illicit drugs and share needles, paraphernalia, and drugs
- people who undergo long-term hemodialysis to treat renal (kidney) failure

- infants born to infected mothers
- people who received organ transplants before 1992 or blood transfusions before 1987 (before stringent screening practices became available)
- people who work in health care and public safety

The most effective measures for protecting against infectious hepatitis are diligent PERSONAL HYGIENE (especially HAND WASHING) and vaccination. Vaccines are available to prevent infection with hepatitis A and hepatitis B. The hepatitis B VACCINE also protects against hepatitis D, which requires the hepatitis B virus to replicate. Hepatitis A and hepatitis E infection confer lifelong immunity. Measures to reduce the risk for noninfectious hepatitis center on eliminating or limiting exposure to hepatotoxic substances including alcohol. The herb MILK THISTLE (silymarin) helps to protect the liver from damage and to recover from damage that occurs. Many health experts recommend that people who have hepatitis or have exposure to hepatotoxins take milk thistle.

See also FOOD SAFETY; HEPATITIS PREVENTION; LIVER CANCER; LIVER DISEASE OF ALCOHOLISM; SHORT BOWEL SYNDROME.

hepatomegaly An enlarged LIVER. Hepatomegaly is a symptom of numerous conditions involving the liver. Its presence or absence has no correlation to the seriousness of the underlying liver disease. Because hepatomegaly is a symptom rather than a condition, it often resolves when the underlying condition comes under control. Chronic liver conditions may result in long-term hepatomegaly.

CONDITIONS THAT CAN RESULT IN HEPATOMEGALY

AMYLOIDOSIS	ANEMIA
CIRRHOSIS	congestive HEART FAILURE
HEMATOCHROMATOSIS	HEPATITIS
INFECTION	infectious mononucleosis
LEUKEMIA	LIVER CANCER
LIVER DISEASE OF ALCOHOLISM	LIVER FAILURE
REYE'S SYNDROME	SARCOIDOSIS
sclerosing cholangitis	STEATOHEPATITIS

See also: HEPATOTOXINS; JAUNDICE; MONONUCLEOSIS, INFECTIOUS; PORTAL HYPERTENSION; SPLENOMEGALY.

hepatotoxins Substances that damage the LIVER. A key role of the liver is to metabolize chemicals that it filters from the BLOOD. In the case of medications, this releases the therapeutic components into the bloodstream and channels the waste byproducts for appropriate elimination. Often the chemical interactions of these metabolic processes generate substances that poison the cells of the liver. Most drugs affect liver function to some degree; hundreds of them have short-term toxic effects and dozens cause permanent liver damage. The most common are ALCOHOL, acetaminophen, and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). Recreational drugs such as hallucinogenic mushrooms are especially hazardous to the liver. Industrial chemicals such as carbon tetrachloride and numerous environmental pollutants also cause the death of liver cells (hepatonecrosis).

Elevated levels of key liver enzymes in the blood provide early indication of hepatotoxicity. These include aspartate aminotransferase (AST), alanine aminotransferase (ALT), and glutamate oxaloacetate transaminase (GOT). Hepatotoxicity may also result in symptoms similar to those of HEPATITIS, such as JAUNDICE, NAUSEA, vomiting, and occasionally FEVER. Damage can be fairly immediate (within days to weeks of ingestion) or manifest months later. Regular alcohol consumption reduces the capacity of the liver to handle toxins, lowering the threshold at which damage occurs. Liver function often returns to normal when ingestion of the toxic substance ends and the liver completes all metabolic functions related to it, though hepatotoxic consequences can cause irreversible loss of liver function and even LIVER FAILURE. Many substances that damage the liver also damage the KIDNEYS. The herb MILK THISTLE, which contains silymarin, helps protect the liver from toxins.

See also ANALGESIC MEDICATIONS; CIRRHOSIS; HALLUCINOGENS; LIVER DISEASE OF ALCOHOLISM; OVERDOSE; POISON PREVENTION; RENAL FAILURE.

hereditary nonpolyposis colorectal cancer (HNPCC) A form of COLORECTAL CANCER predisposed by a mutation in the *mlh1* and *msh1* genes. These genes direct DNA repair mechanisms, the processes cells follow to correct mistakes that occur when they replicate their DNA codes during

cell reproduction, for cells in the mucous membrane lining of the COLON and RECTUM. Having the GENE mutations for HNPCC increases the likelihood that a person will develop colorectal CANCER before the age of 50 years. HNPCC accounts for about 5 percent of colorectal cancer in the United States as well as increased risk for GASTRIC CANCER, ENDOMETRIAL CANCER, and OVARIAN CANCER.

Cancer experts recommend annual COLONOSCOPY (examination of the colon with a flexible, lighted scope) to screen for colorectal cancer when HNPCC mutations are present, beginning at age 20 or upon identification of the mutations. Such screening permits the early detection and removal of the intestinal polyps that are the preliminary foundation for colorectal cancer. Polyps tend to progress to malignancy much faster in people who have genetic predisposition to colorectal cancer. Such aggressive screening has good potential for preventing colorectal cancer. GENETIC TESTING is important as well.

See also ADENOMA-TO-ADENOCARCINOMA TRANSITION; CANCER PREVENTION; CANCER RISK FACTORS; CELL STRUCTURE AND FUNCTION; FAMILIAL ADENOMATOUS POLYPOSIS (FAP); GENETIC DISORDERS; GENETIC TESTING; INHERITANCE PATTERNS; INTESTINAL POLYP.

hiatal hernia A weakening in the DIAPHRAGM, the muscular wall that separates the thoracic cavity (chest) from the abdominal cavity, that allows part of the upper STOMACH to slide upward into the chest. The weakening develops in the natural lapse in the diaphragm's continuity, called the hiatus, that allows the ESOPHAGUS to join the stomach. Hiatal hernia becomes more common with increasing age and often coexists with GASTROESOPHAGEAL REFLUX DISORDER (GERD). Most hiatal hernias do not present symptoms, though the GERD does. The hiatal hernia can worsen the symptoms of GERD by forming a pocket that traps the refluxed gastric contents, intensifying the duration of exposure the esophageal mucosa experiences. Risk factors for hiatal hernia include PREGNANCY (which pressures the diaphragm) and OBESITY.

BARIUM SWALLOW or esophagoscopy (endoscopic examination of the esophagus) can detect the presence of hiatal hernia. Unless there is risk for gastric or esophageal strangulation, in which a portion of the esophagus or stomach becomes pinched off on the thoracic side of the diaphragm, lifestyle modifications such as weight loss and medications to treat associated GERD can successfully manage hiatal hernia. When there is a substantial risk for strangulation, such as with a large hernia, the gastroenterologist may recommend surgery to repair the hernia and prevent strangulation. Gastric or esophageal strangulation, though rare, requires emergency surgery.

See also ACHALASIA; BARRETT'S ESOPHAGUS; ENDOSCOPY; ESOPHAGITIS.

Hirschsprung's disease A CONGENITAL ANOMALY, also called congenital megacolon, in which the nerves that supply the lower COLON, typically the sigmoid colon and RECTUM, are missing. Nerves to the ANUS and anal sphincter are generally intact. The absence of nerves maintains the muscular wall of the lower colon in a state of perpetual contraction, bringing PERISTALSIS to a halt and causing digestive waste to accumulate. These events create pressure in the preceding segments of the colon, causing it to greatly dilate (megacolon). Untreated, this dilation results in TOXIC MEGACOLON, a massive dilation of the colon. Toxic megacolon is a life-threatening emergency that requires immediate surgery.

Symptoms include failure to pass MECONIUM (a newborn's first stool) within 48 hours of birth and ABDOMINAL DISTENTION. Hirschsprung's disease that involves only a short segment of the colon may remain undetected into childhood and even early adulthood, producing primarily symptoms of chronic CONSTIPATION and intermittent abdominal distress. The diagnostic path may include DIGITAL RECTAL EXAMINATION (DRE), abdominal X-rays, ULTRASOUND, or BARIUM ENEMA. Biopsy of the rectal wall confirms the absence of NERVE ganglia.

Treatment is surgery to remove the defective segments of bowel, connecting the ends of healthy bowel to maintain the integrity of the lower intestinal tract. The surgery restores normal bowel motility and function, allowing normal bowel movements. Sometimes the surgery takes place in two operations, the first to remove the defective bowel and the second to reconstruct the colon. A temporary COLOSTOMY allows digestive waste to leave the body during the interim HEALING phase. Most infants who undergo surgical repair before

toxic megacolon develops heal completely and without residual complications. Hirschsprung's disease often coexists with other congenital anomalies, notably DOWN SYNDROME.

See also GENE; INHERITANCE PATTERNS.

H2 antagonist (blocker) medications Medications that block molecular structures called histamine 2 receptors in the lining of the STOMACH. Histamines are chemicals called mediators that stimulate specific cells. Cells within the stomach's lining, called enterochromaffin-like (ECL) cells, release HISTAMINE in response to the digestive HORMONE gastrin. The histamine binds with H2 receptors on the parietal cells in the stomach. This binding stimulates the parietal cells to release hydrochloric acid into the stomach. H2 antagonists, or blockers, bind with the H2 receptors as well, blocking them from binding with endogenous histamine 2. The result is a decrease in acid production.

Other histamines are involved in different body functions. Histamine 1 (H1) stimulates smooth MUSCLE contraction and IMMUNE RESPONSE. H1 is familiar for its role in allergic response. Histamine 3 (H3) has NEUROTRANSMITTER activity. Histamine receptors are primarily unique; only H1 receptors accept histamine 1, only H2 receptors accept histamine 2, and only H3 receptors accept histamine 3. The ANTIHISTAMINE MEDICATIONS to relieve allergy symptoms have no effect on gastric acid production. Similarly, the H2 blockers have no effect on allergies.

Doctors may prescribe H2 blockers to treat GASTROESOPHAGEAL REFLUX DISORDER (GERD), PEPTIC ULCER DISEASE, chronic GASTRITIS, Crohn's disease that involves the stomach and ESOPHAGUS, HIATAL HERNIA, and other conditions in which excessive gastric acid causes symptoms or tissue damage. The four H2 blockers used in the United States are available in over-the-counter (OTC) and prescription strengths.

COMMON H2 BLOCKERS

H2 Blocker	Prescription Strength	OTC Strength
cimetidine (Tagamet)	200mg, 300mg, 400mg, 800mg	100mg
famotidine (Pepcid)	20mg, 40mg	10mg
nizatidine (Axid)	150mg, 300mg	75mg
ranitidine (Zantac)	150mg, 300mg	75mg

H2 blockers, most notably cimetidine, interact with numerous other medications. ANTACIDS prevent the stomach from absorbing H2 blockers, significantly reducing the effectiveness of the H2 blocker. Side effects of H2 blockers may include dizziness, HEADACHE, and DIARRHEA. Changing to a different H2 blocker medication often resolves any side effects.

See also DIGESTIVE HORMONES; PROTON PUMP INHIBITOR (PPI) MEDICATIONS.

I–K

icterus See JAUNDICE.

ileoanal reservoir An operation to connect the ILEUM, the final segment of the SMALL INTESTINE, directly with the anal canal (a short tract immediately before the ANUS) as an alternative to ILEOSTOMY when it is necessary to remove the entire COLON. The surgery may take place in one OPERATION or, more commonly, in two operations. First the surgeon removes the colon, leaving the anal canal, anus, and surrounding muscles intact. Then the surgeon uses the last 18 to 20 inches of the ileum to structure a pouch that replaces the RECTUM, and attaches it to the anal canal. The front end of the ileum remains as part of the small intestine. To allow these changes to heal the surgeon creates a temporary ileostomy, cutting the ileum and bringing the open end through an opening (stoma) in the abdominal wall. The ileostomy allows digestive waste, which, coming from the small intestine is fairly watery, to empty outside the body. When the ileoanal reservoir has healed, the surgeon performs a second operation to reconnect the ends of the ileum within the abdominal cavity and close the ileostomy.

With ileoanal reservoir the person retains control of the anal sphincter and has bowel movements, though stools are soft and bowel movements more frequent (7 to 10 per day). Bulking agents such as methylcellulose (Citrucel) or psyllium (Metamucil) help to solidify the stool. Foods that add bulk to the stool include bananas and rice. Risks of ileoanal reservoir include chronic INFECTION of the pouch, FECAL INCONTINENCE and stool leakage, and the need to make dietary changes (such as cutting out CAFFEINE and milk, which often cause diarrhea). Most people who undergo ileoanal reservoir surgery return to a satisfactory QUALITY OF LIFE.

See also COLOSTOMY; FAMILIAL ADENOMATOUS POLYPOSIS; INFLAMMATORY BOWEL DISEASE (IBD).

ileostomy An OPERATION in which the surgeon brings the end of the ILEUM, the final segment of the SMALL INTESTINE, through the abdominal wall to exit outside the body. A pouch fastens with adhesive to the SKIN around the ileostomal opening, or stoma, to collect digestive waste. The waste is significantly more watery than stool.

An ileostomy is necessary after total bowel resection (removal of the COLON and RECTUM) such as to treat COLON CANCER, and may be temporary or permanent. An ileostomy is temporary when the surgeon can construct an ileoanal reservoir and permanent when this is not a viable option. A variation on an ileostomy that eliminates the need for ostomy bags is the continent ileostomy, in which the surgeon creates a collection pouch from a section of the ileum that remains inside the abdominal cavity. The surgeon sutures a valve in place that exits through the stoma. Periodically the person opens the valve to allow digestive waste to exit.

Many people find the adjustment to an ileostomy challenging. It represents a significant change to the body's appearance and function. The ileostomy, however, need not interfere with the regular activities of life including athletic pursuits, job and career, and sexual activity. An ostomy-care specialist, usually a registered nurse, will provide education about caring for the ileostomy.

See also COLOSTOMY.

ileum The third, final, and longest segment of the SMALL INTESTINE. About 10 feet in length, the

ileum extends from the JEJUNUM to the CECUM. The ileum absorbs fats and fat-soluble vitamins as well as other remaining NUTRIENTS from the digestive content, which it then passes through the ileocecal valve into the cecum (the first segment of the COLON). Like the other segments of the small intestine, the ileum's walls contain extensive villi (fingerlike projections) that expand its surface area to increase its ability to absorb nutrients.

CONDITIONS THAT CAN AFFECT THE ILEUM

Crohn's disease	ILEUS
INTESTINAL ADHESIONS	LYMPHOMA
MALABSORPTION	SHORT BOWEL SYNDROME

For further discussion of the ileum and the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also DUODENUM; ILEOANAL RESERVOIR; ILEOSTOMY; MINERALS AND HEALTH; VITAMINS AND HEALTH; NUTRITIONAL NEEDS.

ileus An obstruction or blockage of the intestinal tract. Ileus is potentially life-threatening and may require emergency surgery. Common causes include

- INTESTINAL ADHESIONS
- tumors (benign or malignant)
- swallowed objects
- severe FECAL IMPACTION
- a BEZOAR that moves into the intestinal tract from the STOMACH

Symptoms include ABDOMINAL PAIN, VOMITING, DIARRHEA, and failure to have bowel movements. Typically BOWEL SOUNDS are absent in the intestinal tract beyond the obstruction, and the abdomen is rigid. The diagnostic path may include abdominal X-RAY, ULTRASOUND, or laparoscopic surgery. Treatment is nearly always surgery to remove the obstruction, often laparoscopic though sometimes OPEN SURGERY is necessary. Delays in surgery can result in tissue necrosis (death), requiring the surgeon to reconstruct a portion of the bowel and increasing the risk of INFECTION.

See also APPENDICITIS; BOWEL MOVEMENT; INTUSSUSCEPTION; MINIMALLY INVASIVE SURGERY; PERITONITIS.

indigestion See DYSPEPSIA.

inflammatory bowel disease (IBD) A chronic disorder in which INFLAMMATION develops along segments of the gastrointestinal tract. There are two forms of IBD, Crohn's disease and ulcerative colitis. Crohn's disease can affect any portion of the intestinal tract though most commonly involves the lower SMALL INTESTINE and upper COLON. Ulcerative colitis affects the colon including the RECTUM. Doctors and researchers believe IBD is an autoimmune disorder in which the IMMUNE SYSTEM may create antibodies that attack the intestinal mucosa (mucus lining of the intestinal walls). Researchers have detected several GENE mutations that correlate to Crohn's disease, and both Crohn's disease and ulcerative colitis have strong familial tendencies. Doctors consider the two conditions collectively because the disease processes, symptoms, and treatments overlap, though each condition has unique clinical features.

Symptoms and Diagnostic Path

Both forms of IBD generate ulcerative sores in the intestinal mucosa that cause irritation and inflammation. The resulting symptoms may include

- DIARRHEA, often bloody when IBD involves the colon
- rectal bleeding
- ABDOMINAL PAIN, sometimes intense
- unintended weight loss
- fatigue
- FEVER

The inflammation and bleeding typically result in ANEMIA, which is one reason for the fatigue. Other systemic changes related to the autoimmune disease process further contribute to fatigue. Alternating periods of symptoms and REMISSION characterize IBD. When IBD is in remission, gastrointestinal function is normal. When the disease is active, often referred to as an "attack," the severity of symptoms may range from manageable to debilitating.

The symptoms typical with IBD also are common with many gastrointestinal disorders. Determining the diagnosis requires a careful history of the pattern of symptoms, thorough physical examination, laboratory tests to look for markers of inflammation and autoimmune activity in the blood and in the stool, and imaging procedures to detect ulcerations and changes in the intestinal mucosa.

BARIUM SWALLOW with small bowel follow-through, in which the radiologist takes additional X-rays to follow the flow of barium as it leaves the STOMACH and passes through the small intestine, can visualize the ulcers and strictures (narrowed areas) that characterize Crohn's disease when it involves the small intestine. Sigmoidoscopy allows visual exploration of the lower colon, the site of ulcerative colitis. Esophagogastroduodenoscopy (EGD) may reveal involvement of the upper gastrointestinal tract in Crohn's disease.

These procedures help rule out other conditions as much as to confirm IBD. Doctors typically withhold these procedures during active flares of disease, however, to avoid further irritating the intestinal mucosa and because the inflamed mucosa presents an increased risk for inadvertent complications such as bowel perforation.

CLINICAL FEATURES OF IBD

Crohn's Disease	Ulcerative Colitis
"skip" pattern of intestinal involvement	continuous intestinal involvement
can affect any part of gastrointestinal tract	affects only the COLON, starts with the RECTUM
infiltrates multiple layers of mucosa	involves only the surface layer of mucosa
right lower abdominal mass	

Treatment Options and Outlook

Most people achieve relief from IBD symptoms through medications that suppress the immune response or target gastrointestinal function. Treatment protocols draw from various classifications of medications to address acute (active disease) and maintenance (remission) levels of care. Among them are ANTIDIARRHEAL MEDICATIONS, anticholinergic medications, 5-AMINOSALICYLATE (5-ASA) MEDICATIONS, CORTICOSTEROID MEDICATIONS, IMMUNOSUPPRESSIVE MEDICATIONS, ANTIBIOTIC MEDICATIONS, and MONOCLONAL ANTIBODIES (MABS). While antibiotics treat enteric infections and abscesses that develop in the inflamed intestinal mucosa, they also seem to reduce complications and result in overall improvement of symptoms.

All of these medications have significant side effects. Because IBD is dynamic and unpredictable in its cycles of symptoms and remission, finding the most effective therapeutic balance remains a challenge. Medication regimens are highly individualized. As research progresses, new medications and treatment options enter the mix.

Surgery to remove the affected portion of the bowel becomes a treatment option to consider when damage to the intestine becomes extensive or symptoms no longer respond to medical treatments. For ulcerative colitis, surgery typically ends the disease process though the amount and location of bowel removed may have functional consequences, including colectomy (surgery to remove part or all of the colon). For Crohn's disease, surgery provides long-term relief though the disease may resurface or progress to involve remaining portions of the gastrointestinal tract.

Lifestyle is an important dimension of IBD not so much for its influence on the course of the disease but rather a result of IBD's influence on lifestyle. IBD is a long-term disorder for which, at present, there is no cure. The unpredictable nature of IBD's cycles and potential severity of attacks make it difficult for those who have it to stray far from its presence. Treatments attempt to manage symptoms for optimal QUALITY OF LIFE across the spectrum of the disease. During periods of remission most people who have IBD are able to participate fully in the activities they enjoy. During periods of active disease, many people find it difficult to maintain regular activities.

Complications associated with IBD are numerous, arising both from the disease and from its treatments. Autoimmune arthritis, notably ANKYLOSING SPONDYLITIS, often develops. Common with long-standing ulcerative colitis are the EYE infections EPISCLERITIS and UVEITIS, the biliary disorder sclerosing cholangitis, and significantly increased risk for COLORECTAL CANCER. Doctors recommend annual screening colonoscopy for people who have IBD with involvement of the colon or rectum beginning 8 to 10 years after diagnosis or earlier

COMMON IBD MEDICATIONS

Drug	Actions
5-aminosalicylates (5-ASAs)	local anti-inflammatory
balsalazide (Colazal)	oral products coated to dissolve in the SMALL INTESTINE or COLON
Canasa suppository	
mesalamine (Asacol, Pentasa)	
olsalazine (Dipentum)	
Rowasa ENEMA	
sulfasalazine (Azulfidine)	
anticholinergics	slow intestinal motility to reduce DIARRHEA
atropine	systemic action
dicyclomine (Bentyl)	
antidiarrheals	slow intestinal motility to reduce diarrhea
loperamide (Imodium)	gastrointestinal action
diphenoxylate (Lomotil)	
antibiotics	treat gastrointestinal INFECTION and abscesses
metronidazole (Flagyl)	
ciprofloxacin (Cipro)	
corticosteroids	systemic anti-inflammatory
budesonide (Encort-EC)	available for intravenous, oral, or rectal administration
hydrocortisone (Hydrocort)	
hydrocortisone enema (Cortenema)	
prednisone	
prednisolone	
immunosuppressives	decrease immune activity
azathioprine (Imuran)	
methotrexate (Amethopterin)	
6-mercaptopurine (Purinethol)	
MONOCLONAL ANTIBODIES (MABS)	blocks action of TUMOR NECROSIS FACTOR (TNFS), which reduces INFLAMMATION
infliximab (Remicade)	

when other risk factors exist. People who have Crohn's disease are particularly susceptible to kidney stones (NEPHROLITHIASIS) and gallstones (cholelithiasis). Abdominal fistulas (abnormal openings between structures), anal fissures, and RECTAL PROLAPSE are also common complications with Crohn's disease. During disease flareups, some people who have IBD develop SKIN conditions.

Risk Factors and Preventive Measures

The most significant risk factor for IBD is family history, and researchers have identified several genes that correspond to the Crohn's disease component of IBD. One in four who has IBD has a first-degree relative (parent, sibling, or child) who also has IBD. There are few other indications for why and how IBD develops, though most doctors believe a combination of factors convene to establish the disease process.

Neither the development nor outbreaks of IBD are preventable. Dietary precautions such as eating small meals and avoiding foods that irritate the gastrointestinal system (such as CAFFEINE, ALCOHOL, and

highly acidic foods) may help maintain overall gastrointestinal health. High-fiber foods often worsen the symptoms of ulcerative colitis and Crohn's disease that involves the colon. People who have IBD generally need NUTRITIONAL SUPPLEMENTS, particularly folic acid (folate) and iron, to offset nutritional deficiencies that result from MALABSORPTION. Smoking exacerbates Crohn's disease. In addition to irritating the gastrointestinal tract, alcohol interacts with many of the medications to treat IBD.

See also ANTIBODY; APPENDICITIS; AUTOIMMUNE DISORDERS; CANCER PREVENTION; CANCER RISK FACTORS; CELIAC DISEASE; COLITIS; DIVERTICULAR DISEASE; ENDOSCOPY; GASTROENTERITIS; GASTROINTESTINAL BLEEDING; ILEUS; IRRITABLE BOWEL SYNDROME (IBS); KAPOSI'S SARCOMA; NUTRITIONAL DEFICIENCY; NUTRITIONAL NEEDS; PERITONITIS.

intestinal adhesions Areas of tissue that fuse together when SCAR tissue extends into normal tissue. Intestinal adhesions are most common in people who have had abdominal surgery (particularly multiple operations) though also may form with ENDOMETRIOSIS, INFLAMMATORY BOWEL DISEASE (IBD), CELIAC DISEASE, and other circumstances in which there is damage to the abdominal tissues that generates scar tissue. Intestinal adhesions may cause abdominal discomfort during certain movements or activities or can become extensive enough to create partial or complete intestinal obstruction (ILEUS). Intestinal adhesions that interfere with digestive functions usually require surgery to clear away the scar tissue. Inherent in this treatment approach, however, is the risk for additional intestinal adhesions to form as a result of the scar tissue that develops during HEALING. Most intestinal adhesions do not cause functional problems. Surgeons typically remove any intestinal adhesions that are present whenever they perform other surgeries.

See also SURGERY BENEFIT AND RISK ASSESSMENT.

intestinal obstruction See ILEUS.

intestinal polyp A fleshy growth, also called an intestinal polypoid ADENOMA, that grows from the mucous membrane lining of the COLON or RECTUM. There are two common types of intestinal polyps, neoplastic adenomas and hyperplastic adenomas, both of which grow almost exclusively in the colon. Neoplastic adenomas are neoplastic (abnormal growths that have no purpose or function in the body) and have the potential to turn malignant. Hyperplastic adenomas are not neoplastic and have no malignant potential.

Adenomas of either type arise from the epithelial cells, which make up the surfaces of membranes as well as the SKIN. Epithelial cells continuously renew themselves to replace worn and damaged epithelial tissues. Protein messengers tell healthy cells when to stop growing, containing the structures they form. When this regulatory mechanism goes awry cells continue to grow, forming abnormal structures such as adenomas. Adenomas, in the intestinal tract as well as elsewhere in the body, become more common with increasing age. Various circumstances converge that permit ADENOMA-TO-ADENOCARCINOMA transition. Though only a small percentage of intestinal polyps become cancerous, more than 95 percent of COLORECTAL CANCER evolves from intestinal polyps. Typically this transition takes 5 to 10 years or longer, during which biopsy can detect the changes in the cells (DYSPLASIA). Cancer experts recommend removal of all intestinal polyps to prevent this evolution. COLONOSCOPY is the most common method for detecting and removing intestinal polyps.

See also ACTINIC KERATOSIS; AGING, GASTROINTESTINAL CHANGES THAT OCCUR WITH; CANCER PREVENTION; CANCER RISK FACTORS; FAMILIAL ADENOMATOUS POLYPOSIS (FAP).

intussusception A circumstance in which one portion of the intestine slides over another in telescopic fashion, creating an intestinal obstruction (ILEUS). Intussusception typically occurs in infants between the ages of 3 and 10 months, though can develop in children up to age six years. It is three times more common in boys than girls.

Intussusception is a life-threatening emergency that requires immediate treatment.

Symptoms include waves (paroxysms) of PAIN that at first appear to be colicky. Within 12 hours, however, the course shifts sharply from that of colic. DIARRHEA and VOMITING develop, and pain

becomes continuous. Stools often are watery and bloody, and may contain large quantities of mucus. Though intussusception is more common in children who have CYSTIC FIBROSIS or Meckel's diverticulum, or who experience blunt trauma to the abdomen, there are no certain predisposing factors.

BARIUM ENEMA provides the diagnosis, and, about 75 percent of the time, the treatment as well because the barium causes the bowel to expand back out. When the intussusception persists, the situation requires immediate surgery. Without treatment intussusception rapidly progresses to PERITONITIS and SEPTICEMIA, and usually is fatal. With appropriate treatment, nearly all infants experience full and uneventful recovery with no long-term consequences. Intussusception typically does not recur.

See also DIVERTICULAR DISEASE.

irritable bowel syndrome (IBS) A constellation of symptoms that reflect functional disturbance of the gastrointestinal system. IBS is one of the most common gastrointestinal disorders that cause people to seek medical care, accounting for 10 percent of doctor visits each year. IBS symptoms are episodic and may range from mild to debilitating and typically manifest before age 35 years. IBS affects three times as many men as women.

Symptoms and Diagnostic Path

The hallmark symptoms of IBS are

- ABDOMINAL PAIN that goes away with bowel movements
- a change in the frequency and nature of bowel movements (DIARRHEA or CONSTIPATION that marks a change from usual bowel movements)
- mucus in the stool (mucorrhea)
- ABDOMINAL DISTENTION or sensation of bloating

Periods of exacerbation alternate with periods of REMISSION. In women, exacerbation may accompany other symptoms of PREMENSTRUAL SYNDROME (PMS). Stress, emotional or physical, is a significant catalyst of symptoms for many people who have IBS. The diagnostic path generally includes the gamut of gastrointestinal tests, though diagnosis of IBS relates to the length of time the person has had symptoms and the frequency with which symptoms occur. Current diagnostic guidelines support a diagnosis of IBS when all of these four symptoms persist for longer than three months and doctors cannot detect any underlying pathologic reasons for the gastrointestinal disturbances.

Treatment Options and Outlook

Treatment targets symptoms and may include ANTIDIARRHEAL MEDICATIONS, ANTICHOLINERGIC MEDICATIONS to slow intestinal motility, and certain ANTIDEPRESSANT MEDICATIONS that are successful in relieving symptoms in CHRONIC PAIN syndromes. Several medications specifically to treat IBS are available. There are significant risks and restrictions for some of these medications, and current regulatory and practice standards limit their use to people whose symptoms fail to respond to other treatments and interfere with daily living.

Alosetron (Lotronex) Alosetron specifically targets the neuroreceptors in the COLON to block the passage of NERVE signals that cause the colon to contract. This slows peristalsis only in the colon, increasing the amount of time digestive matter remains in the colon so the colon can absorb more water from it. Alosetron is available only for use in women who have debilitating diarrhea as the primary component of their IBS and under strict guidelines in which the prescribing doctor and the woman must agree to follow. Alosetron is not available for men because there is insufficient evidence of its effectiveness in men; clinical research studies enrolled primarily women. The most significant risks of alosetron are severe constipation that causes bowel obstruction (ILEUS) and ischemic COLITIS (blocked BLOOD flow to the colon that results in INFECTION).

Tegaserod (Zelnorm) Tegaserod mimics the action of serotonin, increasing the response of serotonin neuroreceptors in the intestinal tract. Serotonin is a NEUROTRANSMITTER most commonly recognized for its role in carrying nerve impulses related to emotion in the BRAIN. However, 95 percent of the serotonin in the body is concentrated in the gastrointestinal tract where it facilitates intestinal motility (peristalsis), gastric acid and other gastrointestinal fluid secretions, and the sensitivity of cells in the gastrointestinal tract to register pain. Like alosetron, tegaserod is available only for use in women who have debilitating diarrhea

and presents the risk of ischemic colitis. Tegaserod also can cause severe diarrhea.

Antidepressants Antidepressant medications affect the actions of several neurotransmitters, such as dopamine and serotonin, that play roles both in brain activity related to emotion and in gastrointestinal functions. The tricyclic antidepressants, such as amitriptyline (Elavil) and imipramine (Tofranil), have been instrumental in treating chronic pain syndromes and provide relief from IBS symptoms for some people. Selective serotonin reuptake inhibitor (SSRI) antidepressants, such as paroxetine (Paxil) and fluoxetine (Prozac), seem to have similar effects. These medications also treat the mild to moderate DEPRESSION that commonly accompanies IBS.

Lifestyle There is a strong correlation between episodes of IBS symptoms and stress. Stress management techniques, MEDITATION, guided imagery, BIOFEEDBACK, YOGA, ACUPUNCTURE, and therapeutic counseling are among the methods that can help keep symptoms in remission. Many people can control IBS largely through diet and lifestyle, after they understand the nature of the disorder and learn to recognize the triggers that bring on attacks of symptoms. Helpful dietary and lifestyle changes include

- reduce or eliminate CAFFEINE, which can contribute to diarrhea
- add fiber by eating more fruits, vegetables, and whole grain products, or by taking a fiber supplement such as psyllium (Metamucil) or methylcellulose (Citrucel)
- eliminate foods and beverages that cause intestinal upset (especially foods high in fat)
- maintain healthy weight
- develop a daily process for stress relief that may incorporate exercise, meditation, warm baths, designated quiet time or alone time, or other methods for de-stressing
- note circumstances and situations that appear to precipitate exacerbations of symptoms and work out approaches to mitigate them
- get 30 to 45 minutes of physical exercise, such as walking, daily to improve circulation, MUSCLE tone, and gastrointestinal function as well as to aid in relieving stress

Risk Factors and Prevention Efforts

Unlike many other chronic disorders affecting the gastrointestinal tract, IBS does not cause any damage to gastrointestinal tissue or increase the risk for CANCER. Even during attacks of symptoms, the bowel shows no evidence of INFLAMMATION or disease process. Tests that measure muscle contraction activity, usually performed only in clinical research studies because they have little diagnostic or therapeutic value, show accelerated peristalsis (intestinal motility).

A significant contingent of researchers and doctors believes IBS has a strong psychological component. This derives in part from the difficulty in identifying any organic, or physical, changes in the gastrointestinal tract that account for the symptoms and in part from a high correlation of diagnosed psychological conditions, such as GENERALIZED ANXIETY DISORDER (GAD) and depression, among people who have IBS. As well, a high percentage of people who have IBS have experienced physical or sexual abuse. Though few argue that these correlations exist, disagreement remains as to what the correlations mean in the context of either the psychological disorder or the IBS, especially in regard to treatment options.

One intriguing direction of research is the exploration of neurohormonal processes that handle both psychological and autonomic (involuntary) functions, raising the possibility of crossover between the two. Some clinical research studies have noted similarities in altered brain activity patterns, as detected via imaging procedures such as POSITRON EMISSION TOMOGRAPHY (PET) SCAN in people who have, independently, clinical depression and IBS. Other directions in research focus on gaining improved understanding of intestinal motility mechanisms. Though for some people IBS is a lifelong condition that requires vigilant management, for many others symptoms abate with an appropriate integration of medical and lifestyle interventions.

See also ACUTE STRESS DISORDER; BOWEL MOVEMENT; CELIAC DISEASE; DIET AND HEALTH; DIVERTICULAR DISEASE; FIBROMYALGIA; INFLAMMATORY BOWEL DISEASE (IBD).

jaundice Yellowish discoloration of the SKIN and whites of the eyes, also called icterus, resulting

from high levels of BILIRUBIN in the BLOOD. As well, the URINE may be dark brown or tea-colored and the stools pale, indicating a high concentration of BILE pigments dissolved in the urine and a lack of bile entering the intestinal tract. Intense itching (PRURITIS) often accompanies jaundice, the skin's reaction to the irritation of the bilirubin deposits. Bilirubin is a byproduct of the destruction of erythrocytes (red blood cells). The SPLEEN performs this destruction to rid the body of old erythrocytes that no longer function properly. The liver incorporates bilirubin into bile, which it then secretes into the gastrointestinal tract to aid in digestion as well as to excrete the excess as waste.

Jaundice indicates liver disease or GALLBLADDER DISEASE that interferes with this bilirubin handling, either in the breakdown stage (liver) or the elimination stage (GALLBLADDER). In most people the jaundice goes away with treatment of the underlying condition. Newborns commonly develop a form of jaundice not related to liver dysfunction called NEONATAL JAUNDICE or physiologic jaundice.

See also CHOLESTASIS; CIRRHOSIS; HEPATITIS.

jejunum The middle segment of the SMALL INTESTINE, between the ILEUM and the DUODENUM. The jejunum is six to eight feet long and handles absorption of carbohydrates and proteins, as well as vitamins such as VITAMIN K and minerals such as iron. The jejunum's tissue composition and excellent blood supply allow it to be the source of tissue grafts for reconstruction of the pharynx and upper ESOPHAGUS after radical surgery to treat laryngeal CANCER (cancer of the THROAT). Health conditions that can involve the jejunum include INFLAMMATORY BOWEL DISEASE (IBD), CELIAC DISEASE, and MALABSORPTION disorders.

For further discussion of the jejunum and the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also BOWEL ATRESIA; SHORT BOWEL SYNDROME.

kernicterus See NEONATAL JAUNDICE.

L

laxatives Products to stimulate bowel movements. Laxatives work through various actions. Some help the stool to retain fluid, keeping the stool softer. Some lubricate the walls of the COLON, making it easier for digestive waste to move through the gastrointestinal tract. Others introduce fiber, which adds bulk to the stool as well as retains more fluid in the stool. Stimulant laxatives irritate the walls of the colon to accelerate PERISTALSIS (contractions of the bowel), which moves stool through the bowel. Laxatives intended to completely clear the colon, such as preparation for BARIUM ENEMA or COLONOSCOPY, are sometimes called cathartics or drastics because their actions are fast and intense. Laxatives come in oral (tablets, powders, and liquids) and rectal (suppositories and enemas) preparations. They are available over the counter.

Doctors recommend attempting natural methods to encourage regular bowel movements before using laxatives. The gastrointestinal tract's rhythm correlates to the kinds and amounts of foods ingested, as well as to the frequency of meals. Though many people believe a daily bowel movement is "normal," normal is an individual measure that can range from two or three times daily to once every three days, depending on dietary habits. Using laxatives to structure daily bowel movements interferes with the bowel's natural rhythms. Over time, the bowel becomes "lazy"

COMMON LAXATIVES

Kind of Laxative	Actions	Representative Products
stool softeners	add moisture to the stool	docusate sodium (Colace) docusate calcium (Surfak)
lubricants	lubricate the intestinal walls	glycerin suppositories mineral oil
bulking agents	add fiber to the stool, which increases bulk and draws moisture	bran calcium polycarbophil (FiberCon) methylcellulose (Citrucel) psyllium (Metamucil)
osmotic agents (hyperosmotics)	draw large amounts of fluid into the stool for rapid and thorough evacuation of intestinal contents	lactulose (Cephulac, Duphalac) magnesium citrate sodium citrate
STIMULANTS	irritate the walls of the colon to cause them to contract (PERISTALSIS)	bisacodyl (Dulcolax) casanthranol (Doxidan) senna (Senokot)

and does not contract unless a laxative stimulates it. Laxatives, and particularly suppositories and enemas, also can irritate the intestinal mucosa enough to cause chronic INFLAMMATION.

See also BOWEL MOVEMENT; DIARRHEA; FIBER AND GASTROINTESTINAL HEALTH; NUTRIENTS; NUTRITIONAL NEEDS; ROUTES OF ADMINISTRATION.

liver The largest internal organ in the body. Its soft, spongy tissue spreads like a flattened football between the DIAPHRAGM and the STOMACH, tucked protectively beneath the lower ribs on the right side of the abdomen. Weighing about three and a half pounds, the liver contains 15 percent of the body's blood (about a pint). About 60 percent of this blood is venous and comes from the gastrointestinal tract and SPLEEN, entering the liver via the portal VEIN. The venous blood delivers nutrients that the liver further metabolizes, the products of which it then sends back into the bloodstream. The hepatic ARTERY, which branches directly from the abdominal AORTA, delivers oxygenated blood to the liver to fuel the functions of its cells. On the underside of the liver is the GALLBLADDER, which concentrates and stores the BILE the liver produces.

The liver's two main lobes, the small left lobe and the large right lobe, support an intricate network of lobules, thousands of tiny communities of hepatocytes (the cells that carry out the liver's functions) that filter NUTRIENTS, wastes, BACTERIA, and toxins from the blood. The microscopic spaces between the lobules are the sinusoids, into which the blood from the portal vein drains. Each lobule is a hexagonal structure two layers of cells deep and several cells horizontally and vertically in a platelike configuration. At the vertical junctions of the lobules are the portal triads, each containing three microscopic structures: a venule, an arteriole, and a bile duct. The portal triads collect the substances the lobules produce and convey them to the larger vessels that will carry them out to the structures of the body. The membranous connective tissue that envelopes the liver also extends like a web through the liver, providing a supportive structure for the lobules, sinusoids, and portal triads.

The lobules are the work stations of the liver. They metabolize nutrients and toxins, and synthesize (manufacture) numerous substances including amino acids, proteins essential for PLASMA production, lipoproteins, cholesterol, immune factors, CLOTTING FACTORS, LYMPH, and bile. The lobules convert GLUCOSE to glycogen, a storage form of glucose the body can draw from when blood levels of glucose fall, and glycogen back to glucose, processes that integrate closely with the balance of glucose and INSULIN in the blood. The lobules also deconstruct old erythrocytes (red blood cells) to recycle the iron and BILIRUBIN they contain. Specialized phagocytic ("cell eating") cells, called Kupffer cells, reside in the sinusoids to consume bacteria and cellular waste. The liver stores iron, glycogen, vitamin A and vitamin B_{12}, and other chemicals the body needs for cellular activities. The liver is unique among the body's organs in its ability to regenerate itself. This extraordinary capacity speaks to the significant extent of damage that must take place to permanently destroy liver tissue. Even so, the liver can meet the needs of the body as long as 25 percent of its cells remain functional.

COMMON CONDITIONS THAT CAN AFFECT THE LIVER

BILIARY ATRESIA	CHOLESTASIS
CIRRHOSIS	DIABETES
HEPATIC ABSCESS	HEPATIC CYST
HEPATITIS	LIVER CANCER
LIVER DISEASE OF ALCOHOLISM	PANCREATITIS
PORTAL HYPERTENSION	PRIMARY BILIARY CIRRHOSIS
PRIMARY SCLEROSING CHOLANGITIS	STEATOHEPATITIS

For further discussion of the liver within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also BILE DUCTS; ESOPHAGEAL VARICES; HEPATOMEGALY; HEPATOTOXINS; JAUNDICE; LIVER FAILURE; LIVER FUNCTION TESTS; LIVER TRANSPLANTATION; NUTRITIONAL NEEDS; VITAMINS AND HEALTH.

liver cancer Malignant growths in the LIVER. Liver CANCER may be primary (originates in the liver) or secondary (metastasizes, or spreads, from other locations in the body). Primary liver cancer is less common than metastatic liver cancer. Most primary liver cancer develops as a complication of chronic HEPATITIS B or hepatitis C INFECTION, conditions that repeatedly damage liver tissue, and

arises from the liver's workhorse cells, the hepatocytes. Hepatocytes continually regenerate; researchers believe the continued replication of the hepatitis VIRUS eventually creates changes in the processes of regeneration (cellular DNA alterations) that cause hepatocyte growth to become uncontrolled. Primary liver cancer is rare in people who have otherwise healthy livers. Because of its rich BLOOD supply and numerous functions related to blood filtration, the liver is a common site for metastatic cancers.

Symptoms and Diagnostic Path

Liver cancer typically does not present symptoms until the cancer is quite advanced, and even then symptoms often are vague. Such symptoms might include upper ABDOMINAL PAIN, ASCITES (fluid accumulation in the abdominal cavity), NAUSEA, lack of APPETITE, and JAUNDICE. The diagnostic path typically includes blood tests to assess liver function and hepatitis status, abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, and PERCUTANEOUS LIVER BIOPSY.

Some doctors advocate regular testing to measure blood levels of ALPHA FETOPROTEIN (AFP), a protein that many liver tumors produce, in people who are at high risk for developing liver cancer (such as those who have chronic hepatitis or severe CIRRHOSIS). However, there is no consensus within the medical community as to the effectiveness of AFP screening for those not at high risk because numerous factors cause erroneous test results.

Treatment Options and Outlook

Treatment for liver cancer depends on whether the cancer is primary or secondary. Treatment for secondary liver cancer is generally palliative, aiming to relieve symptoms such as PAIN. For primary liver cancer, surgical removal of the tumor is the preferred option. However, people who have longstanding cirrhosis may have too much damage for the liver to remain functional after surgery. Large or multiple tumors also are difficult to remove without causing substantial damage to the remaining liver tissue. The surgeon may use RADIOFREQUENCY ABLATION or chemical ablation to kill tumor cells without removing the tumor; this is primarily a palliative treatment. LIVER TRANSPLANTATION is occasionally an option when the liver cancer is primary, small, and well contained.

Conventional external-beam RADIATION THERAPY often is not very successful in altering the course of liver cancer to increase survival, though it can shrink liver tumors to relieve pain and other symptoms. A precise technique for targeting liver tumors with radiation, three-dimensional conformal radiation therapy (3DCRT), shows promise for improving the therapeutic value of radiation therapy in liver cancer. Similarly, conventional CHEMOTHERAPY is not very effective against liver cancer, though in some people directly infusing chemotherapy agents into the hepatic ARTERY, called hepatic artery infusion (HAI) chemotherapy, has therapeutic benefit.

Because liver cancer tends to be either well advanced or metastatic at the time of its diagnosis, the overall outlook remains among the least positive despite the numerous advances in cancer treatments overall. The five-year survival rate, the standard measure for cancer treatment success, is about 30 percent when surgery can remove the tumor and about 5 percent when surgery is not a viable treatment option. Prevention efforts offer the greatest opportunity for defeating liver cancer.

RISK FACTORS FOR LIVER CANCER

anabolic steroid use	chronic arsenic exposure
chronic hepatitis B infection	chronic HEPATITIS C INFECTION
CIRRHOSIS	HEMOCHROMATOSIS
LIVER DISEASE OF ALCOHOLISM	smoking and ALCOHOL abuse in combination
vinyl chloride exposure	
WILSON'S DISEASE	

Risk Factors and Preventive Measures

The most significant risk factor for liver cancer is infection with chronic hepatitis B or hepatitis C. Other circumstances that increase risk include cirrhosis, LIVER DISEASE OF ALCOHOLISM, exposure to hepatotoxic chemicals (especially arsenic, which remains a contaminant in water supplies throughout the United States as a result of past industrial waste practices, and the industrial chemical vinyl chloride), and smoking in combination with ALCOHOL abuse.

The single most important preventive measure for liver cancer is hepatitis vaccination to prevent

hepatitis B infection and appropriate measures to limit exposure to hepatitis C. People who already have chronic hepatitis, cirrhosis, or other conditions that increase the risk for liver cancer, the herb MILK THISTLE (silymarin) may help protect the liver from further damage. Other preventive measures include avoiding circumstances associated with liver cancer, notably excessive alcohol consumption. Though the number of people who develop primary liver cancer is rising, it remains less common than metastatic (secondary) liver cancer.

See also CANCER PREVENTION; CANCER TREATMENT OPTIONS AND DECISIONS; CELL STRUCTURE AND FUNCTION; ENVIRONMENTAL HAZARD EXPOSURE; HEAVY-METAL POISONING; HEPATITIS PREVENTION; METASTASIS; OCCUPATIONAL HEALTH AND SAFETY; SURGERY BENEFIT AND RISK ASSESSMENT.

liver disease of alcoholism Permanent damage to the LIVER that results from long-term, excessive ALCOHOL consumption. Alcohol is one of the most toxic substances ingested into the body. It enters the bloodstream unchanged, about 20 percent absorbed from the STOMACH and 80 percent from the SMALL INTESTINE. The liver must filter alcohol from the blood, a process that certain enzymes in the liver regulate. The enzymes limit the amount of alcohol the liver can extract, allowing alcohol to accumulate in the bloodstream.

The first of these enzymes, alcohol dehydrogenase (ADH), converts the alcohol into acetaldehyde. Acetaldehyde gives the breath of a person who has been drinking alcohol its characteristic odor. It is also a toxin, available as an industrial chemical for numerous manufacturing uses such as a solvent, hardener, and preservative. The second of these enzymes, aldehyde dehydrogenase, facilitates acetaldehyde's break down into acetic acid (the same acid found in vinegar) and acetylcoenzyme A. These substances are less toxic than acetaldehyde. Though aldehyde dehydrogenase works rapidly, it cannot convert all of the aldehyde before this toxic chemical causes the deaths of hepatocytes. Other enzymes in the liver further metabolize the acetic acid and acetate into GLUCOSE (energy) and carbon dioxide (waste).

With repeated exposure to acetaldehyde, structural changes take place in the liver. The first of these is the accumulation of fat in the liver. The liver must direct nearly its full efforts to metabolize alcohol, in the effort to protect itself from the alcohol's toxic effects. As a consequence other metabolic functions in the liver slow, altering carbohydrate and lipid (fat) METABOLISM. The liver can metabolize alcohol at the rate of about 15 grams per hour, a pace that results in minimal hepatocytic damage. Alcohol consumption that exceeds this rate (equivalent to 1 ounce of 100-proof distilled spirits, one 12-ounce beer, or 4 ounces of wine) maintains alcohol circulation in the bloodstream until the liver can accommodate its metabolism. Repeated excessive alcohol consumption characteristically results in three liver disorders, which may exist singly or collectively.

Alcoholic hepatitis The HEPATITIS of ALCOHOLISM, also called Laennec's hepatitis, occurs when the repeated irritation of alcohol results in INFLAMMATION of the liver. When the flow of alcohol through the liver stops, symptoms abate and hepatocytes (the primary working cells of the liver) regenerate. Within a few months of alcohol cessation, the liver can restore itself to a normal level of function.

Alcoholic steatohepatitis Acetylcoenzyme A, one of the products of alcohol metabolism, interferes with the liver's synthesis and storage of fatty acids such that fatty tissue accumulates in the liver. Alcoholic STEATOHEPATITIS improves when the liver's metabolism of alcohol stops, and liver structure can return to normal with alcohol cessation.

Alcoholic cirrhosis Alcoholic CIRRHOSIS is a condition in which repeated INFLAMMATION (hepatitis) causes SCAR tissue to form and replace hepatocytes. As is the case with cirrhosis resulting from any cause, damage that has already occurred to the liver is not reversible. However, alcohol cessation halts the progression of cirrhosis to limit further damage.

Symptoms and Diagnostic Path

The symptoms of alcoholic liver disease are much the same as those of nonalcoholic liver disease and include JAUNDICE (yellowish discoloration of the SKIN), right upper ABDOMINAL PAIN, ASCITES (fluid accumulation in the abdominal cavity), NAUSEA, loss of APPETITE, and FATIGUE. The diagnostic path begins with LIVER FUNCTION TESTS and a thorough assessment of drinking habits. Additional diagnos-

tic procedures might include abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or PERCUTANEOUS LIVER BIOPSY.

Treatment Options and Outlook

Treatment is alcohol cessation and support for symptoms. The doctor may recommend an alcohol and SUBSTANCE ABUSE TREATMENT PROGRAM, counseling, 12-step program such as Alcoholics Anonymous, and other efforts to help maintain SOBRIETY. When liver disease of alcoholism reaches end-stage LIVER FAILURE, LIVER TRANSPLANTATION may be an option for a person who has maintained sobriety for at least six months and has a reasonable expectation of doing so following the liver transplantation. Though liver disease of alcoholism continues if alcohol consumption resumes, with alcohol abstinence the manifestations of liver disease are generally reversible (except cirrhosis).

Risk Factors and Preventive Measures

Chronic alcohol use is the only cause of liver disease of alcoholism. Though most often the use is excessive, alcohol-related damage can occur to the liver with moderate alcohol consumption that extends over a long period of time. Alcoholic steatohepatitis can develop in a person who consumes as few as four alcoholic drinks a week. The only, and absolute, preventive measure is abstinence from alcohol.

See also ENCEPHALOPATHY; HEPATOTOXINS.

liver failure The inability of the LIVER to function. Liver failure may be acute (comes on suddenly) or chronic (develops over time). Because the liver has the unique ability to regenerate, the damage it takes to cause liver failure is substantial. Liver failure generally occurs when more than 75 percent of the liver's hepatocytes, the cells that carry out most of the liver's functions, die, a circumstance called hepatocellular necrosis. LIVER TRANSPLANTATION is the only curative treatment for permanent liver failure.

The most common causes of hepatocellular necrosis leading to liver failure are

- ALCOHOL
- acetaminophen and especially acetaminophen OVERDOSE
- *Amanita* mushroom ingestion
- the illicit DRUG ecstasy (MDMA)
- isoniazid and rifampin in combination to treat TUBERCULOSIS
- industrial chemicals such as arsenic, phosphorus, carbon tetrachloride, and vinyl chloride
- disease processes

Hepatocellular necrosis is a SIDE EFFECT possible with numerous prescription medications, notably certain ANTIBIOTIC MEDICATIONS, "statin" lipid-lowering medications, and tricyclic ANTIDEPRESSANT MEDICATIONS. In some circumstances prompt medical intervention, such as with known overdose of drugs, can slow or halt hepatocellular necrosis and prevent liver failure, though liver damage may still occur. Such interventions might include aggressive medical efforts to remove or neutralize the responsible drug, administration of acetylcysteine for acetaminophen overdose, and liver hemodialysis (though this is of limited availability). In many circumstances, however, the destructive action of the toxin or the inflammatory process overwhelms the liver and attempted medical interventions have little effect.

CONDITIONS THAT CAN CAUSE LIVER FAILURE

BILIARY ATRESIA	chronic HEPATITIS
CIRRHOSIS	HEAT STROKE
HEMATOCHROMATOSIS	HEMORRHAGIC FEVER
LIVER CANCER	LIVER DISEASE OF ALCOHOLISM
PORTAL HYPERTENSION	PRIMARY BILIARY CIRRHOSIS
PRIMARY SCLEROSING CHOLANGITIS	REYE'S SYNDROME
secondary AMYLOIDOSIS	WILSON'S DISEASE

Acute liver failure Acute liver failure, also called fulminant HEPATITIS, develops in days to weeks. It nearly always follows a significant assault to the liver, such as drug overdose or severe trauma (such as gunshot wound) that destroys liver tissue. Hepatitis A INFECTION also can cause acute liver failure. Recovery without liver transplantation is uncommon and is most likely to occur with hepatitis A infection (about 50 percent recovery rate) and promptly treated acetaminophen toxicity.

Chronic liver failure Chronic liver failure, also called nonfulminant hepatitis, develops over

months. Repeated attacks of INFLAMMATION progressively kill hepatocytes until the level of hepatocytic function falls below 25 percent. In many situations a culminating event, such as a flare of hepatitis or an episode of acute alcohol INTOXICATION, pushes the liver across the boundary. CIRRHOSIS is the leading cause of chronic liver failure. Chronic liver failure without liver transplantation is fatal.

Symptoms and Diagnostic Path

People who are in liver failure are very ill. The most prominent symptoms are severe JAUNDICE (yellowish discoloration of the SKIN) and disturbances of cognitive and BRAIN functions, ranging from CONFUSION and HALLUCINATION to COMA, known collectively as hepatic ENCEPHALOPATHY. Neurologic signs that accompany these symptoms include disturbances of reflexes, tremors, and myotonus (MUSCLE spasms and rigidity). Evidence of clotting dysfunction, such as bruising and frank bleeding (internal or external), is also often present as the liver synthesizes many of the proteins and CLOTTING FACTORS necessary for COAGULATION. The diagnostic path includes LIVER FUNCTION TESTS that measure the levels of liver enzymes in the blood, toxicology screens to detect the presence of chemicals in the blood, and imaging procedures of the liver and the brain such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI).

ALCOHOL AND ACETAMINOPHEN: A DANGEROUS COMBINATION

Regular ALCOHOL consumption, even as little as one drink a day, depletes the LIVER's supply of glutathione, an amino acid compound essential for metabolizing toxins. Insufficient glutathione exposes the liver to rapid hepatocellular necrosis, with resulting acute liver failure. People who drink regularly can experience acetaminophen OVERDOSE with as little as 4 grams of acetaminophen a day for three or four consecutive days, an amount that is well within the therapeutic dosage range.

Treatment Options and Outlook

Treatment options for liver failure are primarily supportive. Some people benefit from novel approaches such as liver hemodialysis, which filters the blood similarly to renal dialysis (renal dialysis cannot remove the same substances from the blood), though such methods remain limited to major medical centers. Liver transplantation remains the only viable treatment for permanent liver failure, and the need for donor livers far outpaces the availability of donor organs. In some situations living donor liver segment transplantation, in which a living person donates a segment of his or her liver, is an alternative to cadaver donor liver transplantation.

Risk Factors and Preventive Measures

Chronic hepatitis infection and cirrhosis due to alcoholism are the leading risks for liver failure. Vaccination can prevent much, though not all, hepatitis. Drinking cessation can end the progression of cirrhosis, though damage already done is permanent.

See also ANALGESIC MEDICATIONS; COGNITIVE FUNCTION AND DYSFUNCTION; HEPATOTOXINS; ORGAN TRANSPLANTATION; REFLEX.

liver function tests A panel of BLOOD tests that measures the levels of ALBUMIN, BILIRUBIN, and certain LIVER enzymes in the blood. More specifically targeted tests further identify the reasons for abnormal results, as the findings may also indicate dysfunctions of other organs.

Reasons for Doing This Test

Liver function tests provide a general assessment of how effectively the liver is performing its metabolic tasks. They also allow the doctor to monitor the progression of liver disease and the effectiveness of treatment.

Albumin The liver synthesizes (produces) the key amino acids that make up albumin, the primary protein in blood PLASMA. Albumin transports numerous substances—including other proteins, NUTRIENTS, and hormones—through the blood. When albumin levels are low the blood cannot carry these substances, which has a variety of consequences throughout the body. Many liver conditions cause ASCITES (abdominal edema), in which a deficiency of albumin in the plasma allows plasma to seep across cell membranes to accumulate in the abdominal cavity. Decreased blood albumin

levels suggest liver dysfunction. The normal range of serum albumin is 3.4 to 5.4 grams per deciliter (g/dL).

Bilirubin One key function of the liver is to complete the break down of old erythrocytes (red blood cells) to recycle their ingredients for other uses in the body. The SPLEEN initiates this process, splitting the HEMOGLOBIN erythrocytes contain into its core proteins, heme and globin, and extracting the pigment bilirubin from the heme. Bilirubin is a waste product that the liver chemically alters to use in synthesizing BILE. The chemically processed bilirubin is conjugated or direct bilirubin; bilirubin that circulates in the blood is unconjugated or indirect bilirubin.

A healthy liver excretes most of the conjugated bilirubin it produces in the bile. A damaged liver cannot keep up the pace of bile production, allowing conjugated bilirubin to escape into the blood. Elevated circulation of conjugated, or direct, bilirubin suggests liver or GALLBLADDER dysfunction. The normal range of serum direct bilirubin is 0.0 to 0.4 milligrams per deciliter (mg/dL).

Enzymes Enzymes are catalytic substances that expedite chemical processes within the liver. In a healthy liver enzymes remain within the lobules, the working communities of hepatocytes. Hepatocytic damage results in enzymes leaking from the cells and spilling out into the blood. The commonly measured liver enzymes are

- the aminotransferases (also called transaminases), which catalyze amino acid METABOLISM—for example, aspartate aminotransferase (AST), also called serum glutamic oxaloacetic transaminase (SGOT), and alanine aminotransferase (ALT), also called serum glutamic pyruvic transaminase (SGPT)

LIVER FUNCTION BLOOD TESTS

Blood Test	Normal Values	Liver Implications of Abnormal Findings
ALBUMIN	3.4 to 5.4 grams per deciliter (g/dL)	decreased level may suggest hepatocellular necrosis, HEPATITIS, CIRRHOSIS
alkaline phosphatase (ALP)	44 to 147 International Units per liter (IU/L)	elevated level may suggest hepatitis, cirrhosis, biliary obstruction, LIVER DISEASE OF ALCOHOLISM
alanine aminotransferase (ALT)/serum glutamic pyruvic transaminase (SGPT)	20 to 125 IU/L	elevated level may suggest hepatocellular necrosis, hepatitis, cirrhosis, HEPATOTOXINS
aspartate aminotransferase (AST)/serum glutamic oxaloacetic transaminase (SGOT)	10 to 34 IU/L	elevated level may suggest hepatocellular necrosis, hepatitis, cirrhosis, LIVER CANCER, liver disease of alcoholism
direct BILIRUBIN	0.0 to 0.4 g/dL	elevated level may suggest hepatitis, cirrhosis, biliary obstruction, gallstones, GALLBLADDER DISEASE, CHOLESTASIS
gamma-glutamyltranspeptidase (GGT)	0 to 51 IU/L	elevated level may suggest hepatitis, cirrhosis, liver cancer, cholestasis, hepatocellular necrosis, hepatotoxins
prothrombin time (PT)	11 to 13.5 seconds	delayed time may suggest hepatitis, cirrhosis, gallstones, biliary occlusion

- alkaline phosphatase (ALP), which also goes up in biliary obstruction (blockage of the flow of BILE)
- gamma-glutamyltranspeptidase (GGT)

Collectively elevated levels of these enzymes in the blood indicate damage to the liver that has caused the death of hepatocytes (hepatocellular necrosis). Individual elevations may indicate damage to other tissues in the body such as might occur in the HEART with HEART ATTACK. The AST to ALT ratio is also significant; a ratio greater than 2:1 is common with LIVER DISEASE OF ALCOHOLISM.

Prothrombin time The prothrombin time (PT) measures the amount of time it takes for the clotting process to take place in the plasma. The normal range (for a person who is not taking ANTICOAGULATION THERAPY) is 11 to 13.5 seconds. Clotting time longer than normal suggests a general dysfunction of the body's clotting mechanisms. Liver function becomes suspect with an elevated clotting time because the liver synthesizes many of the proteins (CLOTTING FACTORS) necessary for COAGULATION.

Preparation, Procedure, and Recovery

Liver function tests require a blood sample, typically drawn from a VEIN in the arm. No preparation is necessary and there is no recovery period.

Risks and Complications

Some people experience minor bruising at the site of the venipuncture, which usually heals in a few days (though liver disease that affects clotting mechanisms may extend HEALING).

liver hemodialysis A treatment for acute LIVER FAILURE that employs extracorporeal (out-of-the-body) filtration of the BLOOD to remove the toxins the liver otherwise would metabolize. LIVER hemodialysis is currently of limited availability and remains largely an investigational treatment. Two procedures are in use, the extracorporeal liver assist device (ELAD) and the bioartificial liver. Each uses a biological approach (cultured human cells or porcine cells) to emulate the functions of the liver's hepatocytes (the cells in the liver that filter the blood). These methods provide a "bridge" of limited filtration until liver transplantation becomes possible.

See also CARDIAC ENZYMES; VENTRICULAR ASSIST DEVICES (VADS).

liver transplantation An OPERATION to replace a diseased LIVER with a donor liver as a treatment for end-stage LIVER FAILURE. Following liver transplantation, most people are able to return to full and active lives though must continue taking medications to suppress rejection of the donor liver (IMMUNOSUPPRESSIVE THERAPY).

Surgeons performed the first successful liver transplantation in the United States in 1967. The risk of organ rejection curtailed transplantation as a permanent treatment for liver failure, however, until the advent of the immunosuppressive medication cyclosporine in 1979. Cyclosporine and its contemporary counterparts (such as tacrolimus, which debuted 10 years later) have made transplantation a viable, long-term solution. In 2004 doctors added the monoclonal antibody basiliximab to the immunosuppressive arsenal, reducing rejection to about 10 percent. Surgeons now perform more than 5,500 such operations each year, with liver transplantation as a therapeutic solution limited only by the availability of donor organs.

Donor livers are either cadaveric (harvested from donors after death) or living-donor segment (a living person donates part of his or her healthy liver). Living-donor segment transplantations are possible because the liver has the unique ability to regenerate. After a living donor segment transplantation, the donor's liver eventually restores itself to full size and function. Ideally, the segment implanted in the recipient does the same. This regenerative capability means, too, that livers transplanted into children will grow as the child grows.

There are two basic types of liver transplantation:

- orthotopic liver transplantation (OLT), in which the surgeon removes the diseased liver and replaces it with the donor liver
- heterotopic liver transplantation (HLT), in which the surgeon leaves the person's own diseased liver (the native liver) in place and attaches the donor liver (or liver segment) in a "piggyback" fashion

Donor organs must match BLOOD TYPE and, for OLT, body size. With HLT body size is less important because the surgeon can select a liver segment of the appropriate size. The surgery to transplant a liver takes between 4 and 12 hours in most circumstances. Recovery includes up to three weeks of hospitalization and several months for full recuperation. Most people are able to return to regular activities including exercise, work, sexual activity, and eating habits.

The risks of liver transplantation include bleeding, INFECTION, and rejection of the donor liver. Rejection may occur within days of the transplant or at any time after recovery, though IMMUNOSUPPRESSIVE MEDICATIONS reduce the likelihood. Symptoms of rejection include JAUNDICE, NAUSEA, FEVER, and PAIN. These symptoms require immediate medical attention to salvage the transplant.

CONDITIONS FOR WHICH LIVER TRANSPLANTATION IS AN OPTION

acute (fulminant) LIVER FAILURE	AMYLOIDOSIS
autoimmune HEPATITIS	BILIARY ATRESIA
chronic liver failure	CIRRHOSIS
glycogen storage disease	HEMOCHROMATOSIS
hepatitis B/hepatitis C	hepatotoxic liver failure
LIVER DISEASE OF ALCOHOLISM	noncancerous LIVER tumors
PRIMARY BILIARY SCLEROSIS	PRIMARY SCLEROSING CHOLANGITIS
WILSON'S DISEASE	

See also ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

M–N

malabsorption Inadequate absorption of NUTRIENTS into the BLOOD circulation from the SMALL INTESTINE during digestion, also called malabsorption syndrome. Malabsorption may result from damage to the small intestine that restricts the surface area of the intestinal mucosa (lining) or may develop as a consequence of digestive enzyme deficiencies. CELIAC DISEASE, LACTOSE INTOLERANCE, CYSTIC FIBROSIS, GASTROENTERITIS, and INFLAMMATORY BOWEL DISEASE (IBD) are among the more common causes of malabsorption. Conditions affecting the PANCREAS, LIVER, and GALLBLADDER can result in secondary malabsorption. Untreated malabsorption characteristically causes NUTRITIONAL DEFICIENCIES and MALNUTRITION.

The diagnostic path may include stool analysis, blood tests, and URINALYSIS. The gastroenterologist may perform an ENDOSCOPY with biopsy when preliminary test findings are inconclusive. Treatment, which often includes a combination of dietary and medical management methods, targets any underlying condition. Secondary malabsorption generally goes away when the underlying condition improves. Severe malabsorption with malnutrition requires PARENTERAL NUTRITION (intravenous solutions) to replenish the body's nutrients. Malabsorption related to enzyme deficiencies often resolves with dietary changes alone.

See also BORBORYGMUS; DIET AND HEALTH; DIGESTIVE ENZYMES; NUTRITIONAL NEEDS; PANCREATITIS; SHORT BOWEL SYNDROME; SMALL BOWEL TRANSPLANTATION; STEATORRHEA; WHIPPLE'S DISEASE.

meconium The first stool a newborn passes, made up of AMNIOTIC FLUID, BILE, and mucus. Meconium resembles tar in consistency and color. Its passing is a key indictor of the infant's health and gastrointestinal patency (clear passage). Infants with healthy gastrointestinal systems pass their first meconium stools within 24 hours of birth and may continue to pass meconium for two or three days. An infant that fails to pass meconium within 24 hours may have a congenital malformation of the gastrointestinal tract such as BOWEL ATRESIA. A complication common in infants who have CYSTIC FIBROSIS, a genetic disorder that affects multiple body systems, is meconium ILEUS in which impacted meconium obstructs the bowel. Enemas often relieve the impaction; when they do not, surgery is necessary.

See also CHILDBIRTH; CONGENITAL ANOMALY; ENEMA.

nasogastric aspiration and lavage The clinical term for the procedure commonly called "pumping the STOMACH." In nasogastric aspiration and lavage, the health-care provider inserts a narrow tube (catheter) through the NOSE, down the back of the THROAT and the ESOPHAGUS, and into the stomach. The stomach's contents are then sucked through the tube. The health-care provider may also use the tube to instill a rinsing solution, often a mixture of liquid and activated charcoal, into the stomach to absorb and neutralize remaining gastric content. Nasogastric aspiration and lavage is most commonly an emergency treatment for ingested toxins, including DRUG OVERDOSE, though also can help diagnose gastric bleeding.

See also GASTROINTESTINAL BLEEDING; INGESTED TOXINS.

nausea A sensation of queasiness and the feeling of being about to vomit. Though nausea feels as though it arises from the gastrointestinal tract, the signals that initiate its sensations originate in two areas of the BRAIN, the chemoreceptor trigger zone and the emetic (VOMITING) center. These areas are

bilateral, existing in pairs on each side of the brain. Both receive NERVE and chemical input from body systems. Nausea often precedes vomiting, the forceful expulsion of upper gastrointestinal contents. However, nausea also exists without resulting in vomiting. Many medications that suppress nausea and vomiting, called ANTIEMETIC MEDICATIONS, block the chemical and nerve signals entering or leaving the chemoreceptor trigger zone.

Nausea is typically a symptom, a reaction such as a medication SIDE EFFECT, or a response such as to an irritation of the gastrointestinal tract. Severe PAIN such as from migraine HEADACHE, HEART ATTACK, MENINGITIS, or injury (including postoperative pain) also activates the chemoreceptor trigger zone and the emetic center. The causes of nausea send different kinds of signals. Some antiemetic medications, such as prochlorperazine (Compazine) and meclizine (Antivert), generally target a broad range of these signals. Other medications, such as those prescribed to treat CHEMOTHERAPY-induced nausea and vomiting (CINV) or radiation-induced nausea and vomiting (RINV), narrowly and specifically target certain chemoreceptors.

ACUPUNCTURE, an ancient Eastern method in which the practitioner inserts hairlike needles in designated locations, is highly effective for some kinds of nausea including CINV, RINV, motion sickness, and MORNING SICKNESS. Acupressure, which uses pressure applied over key acupuncture points, is also effective for many people. Other remedies for nausea include GINGER and "flat" cola drinks or cola syrup.

See also CYCLIC VOMITING SYNDROME; FOOD-BORNE ILLNESSES; GASTROENTERITIS.

P

pancreas An elongated gland with both endocrine and exocrine functions that lies beneath the STOMACH on the upper left side of the abdomen, beneath the lower ribs. Both realms of function play roles in digestion, though the endocrine functions of the pancreas are also significant for maintaining the body's GLUCOSE-INSULIN balance and for regulating cellular use of glucose.

The main body of the pancreas is a loose collection of secretory cells, looking somewhat like a mass of fish eggs, that produce DIGESTIVE ENZYMES and juices. These cells organize in lobular formations, called acini, around ducts that channel their secretions to the main pancreatic duct coursing through the center of the pancreas (hence their designation as exocrine). The pancreatic duct joins the common BILE duct from the GALLBLADDER just before the DUODENUM (the first segment of the SMALL INTESTINE), adding its juices to the bile that then flows into the duodenum.

Interspersed among the secretory cells are about a million clusters of specialized cells that produce the hormones INSULIN, GLUCAGON, and SOMATOSTATIN. Called the ISLETS OF LANGERHANS, these clusters are the endocrine glands of the pancreas. An extensive BLOOD supply infiltrates the islets, which secrete their hormones directly into the bloodstream (hence their designation as endocrine). These hormones regulate numerous functions of METABOLISM throughout the body, including many that take place in the gastrointestinal system.

Pancreatic Enzymes and Juices

The pancreas produces numerous enzymes essential for digestion. DIGESTIVE HORMONES trigger their release. Key among the digestive enzymes are

- proteases, notably trypsin and chymotrypsin, which break down proteins; to protect itself from these proteases hydrolyzing its own tissue, the pancreas secretes them in proenzyme forms, trypsinogen and chymotrypsinogen, that an enzyme in the duodenum, enterokinase, activates
- pancreatic lipase, which breaks down dietary triglyceride into fatty acid molecules the intestinal mucosa can absorb
- amylase, which breaks down dietary starches (plant-based stored carbohydrates) into disaccharides (multiple molecule sugars) in preparation for further digestion later in the small intestine
- ribonuclease and deoxyribonuclease, which break down nucleic acids (chemicals that facilitate the body's use of proteins)
- elastase, which facilitates the break down of proteins into amino acids
- bicarbonate, which neutralizes gastric acid in the chyme (mixture of food and gastric juices) that flows from the stomach into the duodenum

Pancreatic Hormones

The primary hormones the pancreas produces are insulin, glucagon, and somatostatin. Insulin is key to carbohydrate and lipid (fatty acid) metabolism, in the gastrointestinal tract as well as at the cellular level throughout the body. The pancreas releases insulin in response to digestive hormones the gastrointestinal tract secretes as food enters the various stages of digestion. Insulin regulates glucose levels in the blood by controlling how much, and when, glucose enters the cells. It also signals the LIVER to convert excess glucose to the storage form glycogen. Somatostatin slows the release of insulin. Glandular tissue in the intestinal mucosa also produces somatostatin, which

acts to slow the release of other digestive enzymes as well. The pancreas releases glucagon when blood glucose levels fall. Glucagon signals the liver to convert glycogen to glucose.

COMMON CONDITIONS THAT CAN AFFECT THE PANCREAS

DIABETES	gallstones in the common bile duct
PANCREATIC CANCER	pancreatic cyst
pancreatic pseudocyst	PANCREATITIS

For further discussion of the pancreas and the functions of the islets of Langerhans within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also DIABETES; DIET AND HEALTH.

pancreatic cancer Malignant growths of the PANCREAS. Pancreatic CANCER seldom shows symptoms until the cancer is well advanced or metastasized, making it among the most lethal cancers and the fourth leading cause of deaths from cancer in the United States. The one-year survival rate is about 24 percent.

When symptoms do appear as the cancer advances, they include

- JAUNDICE, a yellowish discoloration of the SKIN that results from the cancer compressing the common bile duct and blocking the flow of BILE into the DUODENUM
- ABDOMINAL PAIN that may radiate to the back
- digestive disturbances that result from the cancer's interference with pancreatic enzyme production or blockage of the ducts that carry the secretions out of the pancreas

The diagnostic path includes imaging procedures such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or POSITRON EMISSION TOMOGRAPHY (PET) SCAN to determine the location and extent of the cancer as well as LYMPH NODE involvement and regional METASTASIS. Percutaneous (needle) biopsy confirms the diagnosis.

Treatment depends on how extensively the cancer has spread. Surgery is most effective when the cancer is small, remains confined to the pancreas, and is located in the head of the pancreas. Pancreatectomy, partial or complete, is complex surgery with significant risks and consequences (including DIABETES). It is a viable option only when the surgeon is reasonably certain it will completely remove the cancer. About 90 percent of pancreatic cancers have metastasized by the time of diagnosis. CHEMOTHERAPY may be effective in achieving REMISSION. External beam RADIATION THERAPY can shrink the cancer to relieve symptoms.

There are few clear risk factors or screening procedures for pancreatic cancer. There is some evidence of a hereditary component to pancreatic cancer, as it appears to run in families, though researchers have yet to detect the responsible genes. In people at high risk for developing pancreatic cancer because of family history, some cancer experts suggest annual ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP). This endoscopic procedure allows the gastroenterologist to examine the pancreatic duct for signs of precancerous changes in the cells (DYSPLASIA). Areas of focus in research include GENE THERAPY and IMMUNOTHERAPY (also called biological therapy), though therapeutic application of these remains investigational.

See also CANCER TREATMENT OPTIONS AND DECISIONS; ENDOSCOPY; LYMPH NODES; PANCREATITIS; RISK FACTORS FOR CANCER; STOMACH CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

pancreatitis INFLAMMATION of the PANCREAS that can be acute (comes on suddenly) or chronic (ongoing).

Acute pancreatitis can be life-threatening and requires emergency medical treatment.

Between them, excessive ALCOHOL consumption and gallstones account for more than 80 percent of pancreatitis. Other causes include CYSTIC FIBROSIS, viral INFECTION (notably with the MUMPS VIRUS), SIDE EFFECTS of certain medications, and trauma to the abdomen (particularly blunt trauma such as might occur in MOTOR VEHICLE ACCIDENTS). A good deal of the time doctors cannot identify the cause of pancreatitis.

Symptoms and Diagnostic Path

Acute pancreatitis makes a person very ill, with symptoms that include moderate to severe ABDOMINAL PAIN, ABDOMINAL DISTENTION; NAUSEA, VOMITING, and FEVER. Often the PULSE and respiration rate are rapid. When symptoms are severe, the person may be in SHOCK, which is a life-threatening emergency. The diagnostic path includes BLOOD tests to measure the levels of the DIGESTIVE ENZYMES amylase and lipase, which become significantly elevated with pancreatitis. ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) can often identify signs of inflammation and can help determine whether gallstones are obstructing the BILE DUCTS, a common cause of acute pancreatitis. ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN also can provide therapeutically useful information.

People who have chronic pancreatitis may have intermittent upper ABDOMINAL PAIN, though with advanced damage to the pancreas pain is less common. The primary symptom of chronic pancreatitis is persistent weight loss despite adequate eating. This occurs because the damaged pancreas is unable to produce the digestive enzymes the SMALL INTESTINE needs to absorb nutrients, so consumed food passes through the gastrointestinal tract largely useless in the context of meeting the body's NUTRITIONAL NEEDS. The same procedures doctors use to diagnose acute pancreatitis help diagnose as well as monitor chronic pancreatitis. Specialized tests also can measure production of pancreatic enzymes.

Treatment Options and Outlook

Treatment for acute pancreatitis is primarily supportive, with intravenous fluids to restore fluid and electrolyte balance within the body as well as to deliver GLUCOSE. Surgery becomes necessary when there is bleeding in the pancreas. Though illness can be severe, most people recover without residual consequences. Some people do subsequently develop chronic pancreatitis. Other complications may include RENAL FAILURE and the development of fluid-filled pockets called pseudocysts that often become infected.

Treatment for chronic pancreatitis is elimination of any contributing factors (such as alcohol consumption or removal of gallstones), plus a high-carbohydrate, low-fat diet to get basic nutrients into the body. Enzyme supplements can improve digestion. Complications include DIABETES (requiring INSULIN THERAPY) and progressive loss of pancreatic function.

Risk Factors and Preventive Measures

Excessive alcohol consumption and gallstones are the leading risk factors for pancreatitis; alcohol abstinence and appropriate treatment for gallstones eliminates them. Other causes of pancreatitis are less defined and thus more difficult to prevent. Prompt medical assessment of symptoms and appropriate treatment improve the likelihood for uneventful recovery.

See also ALCOHOLISM; ENDOSCOPY; PANCREATIC CANCER.

peptic ulcer disease A condition in which ulcers form in the lining (mucosa) of the lower STOMACH and upper DUODENUM (first segment of the SMALL INTESTINE). The two most common causes of peptic ulcer disease are INFECTION with *HELICOBACTER PYLORI* and chronic or long-term use of NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). Peptic ulcer disease affects millions of Americans. In most situations, appropriate treatment cures the condition.

Symptoms and Diagnostic Path

The symptoms of peptic ulcer disease range from mild and intermittent to severe and unrelenting. Severe symptoms suggest a perforated ulcer, which carries the risks of bleeding and infection. A perforated ulcer requires immediate medical attention.

Typical symptoms of peptic ulcer disease include

- DYSPEPSIA (heartburn or stomach upset), commonly occurring one to three hours after eating or at night
- NAUSEA and VOMITING
- GASTROINTESTINAL BLEEDING
- loss of APPETITE or intolerance for spicy or fatty foods
- unintended weight loss

Symptoms typically improve with ANTACIDS or acid-reducing medications. Some people experience CHEST PAIN mistaken for HEART ATTACK.

ENDOSCOPY to examine the ESOPHAGUS, stomach, and duodenum often makes the diagnosis, allowing the gastroenterologist to visualize the ulcers and extent of damage. Biopsy of a tissue sample or an urea breath test can determine whether *H. pylori* infection is present.

Treatment Options and Outlook

H. pylori infection accounts for nearly 80 percent of peptic ulcer disease. Treatment with appropriate ANTIBIOTIC MEDICATIONS to eradicate the BACTERIA allows the ulcers to heal. Chronic NSAID use is the second-most common cause of peptic ulcer disease; ulcers typically heal when the person stops taking the NSAID. Regardless of cause, the treatment of choice for peptic ulcer disease is acid-reducing medication to decrease irritation to the damaged tissue.

Gastroenterologists typically prescribe H2 ANTAGONIST (BLOCKER) MEDICATIONS or PROTON PUMP INHIBITOR (PPI) MEDICATIONS for this purpose. After the ulcers heal, most people no longer need to take the medication. Severe ulcers may require surgery, particularly if they are bleeding. The primary complication of peptic ulcer disease is perforation (an ulcer that "eats through" or penetrates the wall of the duodenum or stomach), which can result in life-threatening bleeding and usually requires surgery. There also is some evidence linking long-term peptic ulcer disease, particularly that resulting from *H. pylori* infection, with an increased risk for STOMACH CANCER.

Risk Factors and Preventive Measures

Doctors once believed stress was the primary cause of peptic ulcer disease, though now know this is not the case. The causes of peptic ulcer disease, are largely treatable (*H. pylori* infection) or preventable (NSAID overuse).

See also GASTROESOPHAGEAL REFLUX DISORDER (GERD); MULTIPLE ENDOCRINE NEOPLASIA (MEN); RISK FACTORS FOR CANCER; ZOLLINGER-ELLISON SYNDROME.

percutaneous liver biopsy A diagnostic procedure for removing a tissue sample from the LIVER. The doctor typically performs percutaneous liver biopsy on an outpatient basis in a hospital setting. Most people prefer to receive a mild sedative before the procedure. After anesthetizing the abdominal SKIN and tissue above the liver, the doctor makes a tiny incision and inserts a special biopsy needle. The needle withdraws a core of liver tissue, which a laboratory then analyzes to determine the nature and structure of cells and other substances it contains. Percutaneous liver biopsy helps diagnose numerous conditions affecting the liver, including HEPATITIS, CIRRHOSIS, LIVER FAILURE, STEATOHEPATITIS, and LIVER CANCER. Though minimally invasive, percutaneous liver biopsy exposes the liver to several risks including INFECTION, INFLAMMATION, and bleeding. These complications are uncommon though can be serious.

See also LIVER FUNCTION TESTS.

peristalsis The rhythmic waves of contraction that move food through the gastrointestinal tract. Pressure against the inner walls of the intestines, such as occurs when food enters an intestinal segment, signals the muscles to contract and relax in a progressive pattern. The muscles ahead of the pressure relax, widening the intestinal passage, and the muscles behind the pressure contract, narrowing the passage. This action "massages" the intestinal contents forward. Peristalsis is totally involuntary, under the control of the autonomic NERVOUS SYSTEM.

See also BORBORYGMUS; BOWEL SOUNDS.

peritonitis INFLAMMATION and INFECTION of the peritoneal membrane that encases the contents of the abdominal cavity. Peritonitis usually indicates a perforation of the intestinal tract that allows intestinal content, including normally present BACTERIA, to spill into the abdominal cavity. Such a breach may occur as the result of APPENDICITIS or COLITIS, or with INFLAMMATORY BOWEL DISEASE (IBD) or DIVERTICULAR DISEASE that erodes through the wall of the intestine. Peritoneal ABSCESS also often causes peritonitis. Peritoneal dialysis for KIDNEY failure, which circulates fluid within the peritoneal cavity to draw toxins from the body, may introduce bacteria into the peritoneal cavity to cause peritonitis.

Peritonitis is potentially life-threatening and requires emergency treatment and usually surgery.

Symptoms often appear suddenly and are severe. Initially the perforation may provide relief because it releases pressure but the spreading infection quickly worsens symptoms. There is often abdominal rigidity and guarding (extreme resistance to having anyone touch the abdomen), ABDOMINAL DISTENTION, high FEVER, and signs of SEPTICEMIA (septic SHOCK) such as rapid PULSE and respiration. Blood tests and abdominal X-RAY or ULTRASOUND generally confirm the diagnosis. The infection paralyzes the intestine, halting PERISTALSIS and the absorption of fluids, nutrients, and electrolytes. Electrolytes are critically important for proper regulation of many body activities including those of the BRAIN and HEART. Treatment is immediate intravenous fluids to restore the body's electrolyte balance, ANTIBIOTIC MEDICATIONS to begin fighting the infection, and usually emergency surgery to drain the infection from the peritoneal cavity and remove any necrotic (dead) tissue or bowel. Recovery is not certain, and often complications remain following treatment, depending on the reason for the peritonitis.

See also PELVIC INFLAMMATORY DISEASE (PID); RENAL DIALYSIS.

portal hypertension High pressure in the portal VEIN, the large BLOOD vessel that carries blood from the abdominal organs to the LIVER. CIRRHOSIS, in which SCAR tissue replaces liver tissue as a consequence of repeated INFLAMMATION, is the primary cause of portal hypertension. Right HEART FAILURE also can cause portal hypertension.

About 40 percent of the blood that enters the liver does so through the portal vein. Blood drains into the portal vein from the digestive organs of the abdomen, carrying NUTRIENTS and metabolic wastes to the liver for processing. Though blood flows through the arteries under high pressure, the pressure within the veins is low and venous blood flow mostly relies on a combination of lower resistance, gravity, and valves within the veins to prevent backflow.

The spongy tissue of a healthy liver accepts blood flow from the portal vein in a smooth process, literally soaking in the blood and channeling it through the thousands of lobules that form the liver's interior architecture. The solid structure of scar tissue does not absorb blood like the spongy tissue of the healthy liver, and blood must force its way around. The resistance that results causes the pressure within the portal vein to rise.

When scarring becomes severe, as in cirrhosis, the liver cannot contain the amount of blood attempting to enter and the blood backs up into the portal vein as well as the veins that feed into the portal vein. The walls of the portal vein stiffen against the resistance, which further raises pressure. Eventually the consequence of portal hypertension is twofold: blood cannot circulate through the liver and the supporting veins that feed into the portal vein distend and weaken. These VARICOSE VEINS typically protrude into the ESOPHAGUS (ESOPHAGEAL VARICES) and often bleed.

Symptoms and Diagnostic Path

The key symptoms suggesting portal hypertension are those of liver disease and may include

- JAUNDICE, a yellowish discoloration of the SKIN
- PRURITUS (widespread itching)
- fatigue and weakness
- ASCITES, an accumulation fluid in the abdomen
- evidence of GASTROINTESTINAL BLEEDING, which may appear as VOMITING blood (hematemesis) or passing dark stools (melena)

The doctor's examination can usually detect numerous signs of portal hypertension, such as abnormal PULSE, low systemic BLOOD PRESSURE (HYPOTENSION), and evidence of altered venous blood flow in the abdomen and lower extremities. The diagnostic path includes imaging procedures that can show the flow of blood through the liver, such as Doppler ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI). Endoscopic examination of the esophagus reveals esophageal varices, a conclusive sign of portal hypertension.

Treatment Options and Outlook

Bleeding esophageal varices require immediate medical attention. The gastroenterologist often can cauterize these during ENDOSCOPY. Vasodilator medications that relax the blood vessels, such as nitrates and beta blockers, relieve mild to moderate portal hypertension. Moderate to severe portal

hypertension requires surgical intervention. Shunts can help redirect the flow of blood into the liver and lower portal vein pressure. Sometimes removing the SPLEEN (SPLENECTOMY) and blood vessels surrounding the esophagus is necessary to control esophageal varices. The only curative treatment is LIVER TRANSPLANTATION, which, because donor organs are so limited, is a treatment of final resort when other therapies fail and LIVER FAILURE becomes life-threatening.

Medications and intermediary surgical procedures such as shunts can successfully manage portal hypertension in many people, allowing good QUALITY OF LIFE.

Risk Factors and Preventive Measures

Chronic liver disease and heart disease are the primary risk factors for portal hypertension. Lifestyle measures to minimize these conditions, and appropriate treatments to manage them when they do occur, significantly reduce the likelihood that portal hypertension will develop.

See also CARDIOVASCULAR DISEASE PREVENTION; HEMOCHROMATOSIS; HEPATITIS PREVENTION; LIFESTYLE AND HEALTH; WILSON'S DISEASE.

primary biliary cirrhosis An autoimmune disorder in which chronic and progressive INFLAMMATION destroys the intrahepatic BILE DUCTS (bile ducts within the LIVER), blocking the flow of BILE. Primary biliary CIRRHOSIS appears to run in families, suggesting a hereditary component. Early symptoms include fatigue, tenderness or PAIN in the upper right abdomen, and itching (PRURITIS). Over time, signs of liver damage, such as JAUNDICE and HEPATOMEGALY (enlarged liver), emerge. Primary biliary cirrhosis is most common in women between the ages of 40 and 60.

The diagnostic path includes

- LIVER FUNCTION TESTS, which typically show elevations of the enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyl transpeptidase (GGTP).
- BLOOD tests to measure the level of immunoglobin (elevated) and detect the presence of antimitochondrial antibodies (positive)
- imaging procedures such as abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI)
- PERCUTANEOUS LIVER BIOPSY

The progressive destruction of the bile ducts results in CHOLESTASIS and cirrhosis, leading ultimately to LIVER FAILURE. Complications include OSTEOPOROSIS (arising from the body's inability to metabolize vitamin D and calcium), PORTAL HYPERTENSION, ESOPHAGEAL VARICES, and primary LIVER CANCER.

There are currently few medical treatment options. The medication ursodiol (Actigall), sometimes taken to help dissolve gallstones, slows the progression of the inflammatory process in some people. ANTIHISTAMINE MEDICATIONS can help relieve the itching in the early stages; in later stages some people experience relief from itching with bile sequestrant medications such as cholestyramine and colestipol, which bind with bile in the gastrointestinal tract. The only curative treatment, however, is LIVER TRANSPLANTATION.

See also AUTOIMMUNE DISORDERS; BILIARY ATRESIA; CANCER RISK FACTORS; GALLBLADDER DISEASE; PRIMARY SCLEROSING CHOLANGITIS.

primary sclerosing cholangitis A progressive and chronic condition in which segments of the BILE DUCTS become inflamed, causing SCAR tissue (sclerosis) that narrows and stiffens them. The scarring reduces and eventually destroys the ability of the ducts to carry BILE. About 75 percent of people who have primary sclerosing cholangitis also have INFLAMMATORY BOWEL DISEASE (IBD), suggesting a related autoimmune process. Primary sclerosing cholangitis is most common in men between the ages of 20 and 40.

In the early stages of the disease symptoms are mild and tend to wax and wane. Early symptoms may include fatigue, tenderness or PAIN in the upper right abdomen, and mild JAUNDICE (yellowish discoloration of the skin). Often the discovery of primary sclerosing cholangitis comes with elevated enzyme levels on LIVER FUNCTION TESTS done for other reasons, with confirmation by imaging procedures, such as ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, and PERCUTANEOUS LIVER

BIOPSY. As more damage to the bile ducts occurs, symptoms intensify.

Medical interventions for primary sclerosing cholangitis are primarily supportive and aim to relieve symptoms such as PRURITIS (intense itching), which become more prominent as the condition progresses. The damage ultimately results in CIRRHOSIS and LIVER FAILURE. A significant risk during this progression is cholangiocarcinoma, a cancerous tumor that develops in the inflamed bile ducts. The course of the disease varies though tends to run about 10 years from onset of symptoms to liver failure. The only curative treatment is LIVER TRANSPLANTATION.

See also AUTOIMMUNE DISORDERS; BILIARY ATRESIA; CANCER RISK FACTORS; GALLBLADDER DISEASE; PRIMARY BILIARY CIRRHOSIS.

proctitis INFLAMMATION of the RECTUM that may also involve the ANUS. A number of circumstances may cause proctitis, including

- INFECTION, notably SEXUALLY TRANSMITTED DISEASES (STDS) such as CHLAMYDIA, GONORRHEA, and GENITAL HERPES
- inflammatory conditions such as INFLAMMATORY BOWEL DISEASE (IBD) and DIVERTICULAR DISEASE
- trauma to the anus and rectum
- bacterial INFECTION secondary to chronic inflammation or trauma
- RADIATION THERAPY (radiation proctitis)

Symptoms include the continuous sensation of needing to have a BOWEL MOVEMENT, CONSTIPATION, and rectal discomfort or PAIN. The doctor can usually diagnose proctitis via proctoscopy (viewing the anus and rectum endoscopically). Treatment targets the cause, which may include ANTIBIOTIC MEDICATIONS for infections and CORTICOSTEROID MEDICATIONS or other anti-inflammatory products for inflammation arising from trauma, radiation therapy, and inflammatory conditions of the gastrointestinal tract.

See also ANAL FISSURE; ENDOSCOPY; HEMORRHOIDS.

proton pump inhibitor (PPI) medications Medications that suppress gastric acid production in the STOMACH. Commonly prescribed PPIs available in the United States include

- esomeprazole (Nexium)
- lansoprazole (Prevacid)
- omeprazole (Prilosec)
- pantoprazole (Protonix)
- rabeprazole (Aciphex)

How These Medications Work

PPIs work by blocking the enzyme system that causes the parietal cells in the stomach's lining (gastric mucosa), called proton pumps, to produce and release hydrochloric acid. PPIs can block up to 99 percent of gastric acid production. PPIs also appear to slow the ability of *HELICOBACTER PYLORI* bacteria to move, reducing their ability to cause INFECTION. *H. pylori* infection is responsible for up to 80 percent of ulcers.

Therapeutic Applications

Doctors prescribe PPIs to treat PEPTIC ULCER DISEASE, GASTROESOPHAGEAL REFLUX DISORDER (GERD), and other conditions in which gastric acid becomes an irritation that causes symptoms such as INFLAMMATION and PAIN. PPIs are intended for relatively short-term use, during the HEALING phase of damaged gastrointestinal mucosa. After healing is complete, doctors recommend dietary modifications and H2 ANTAGONIST (BLOCKER) MEDICATIONS or ANTACIDS for people who still need to suppress gastric acid.

Risks and Side Effects

PPIs have relatively few side effects or risks. Among the most common are HEADACHE, dizziness, fatigue, NAUSEA, ABDOMINAL PAIN, and DIARRHEA. No one PPI is more likely than another to cause side effects. Pregnant women should not take PPIs because researchers do not yet know whether these medications can harm the developing FETUS.

See also ESOPHAGITIS; GASTRITIS; GASTROENTERITIS.

R

rapid gastric emptying A disorder, also called dumping syndrome, in which food moves from the STOMACH into the SMALL INTESTINE incompletely digested, resulting in the small intestine attempting to digest solid food particles. Normally the digestive content that reaches the small intestine is fairly liquefied. The incomplete gastric digestion causes various gastrointestinal symptoms and leads to MALABSORPTION. Rapid gastric emptying typically occurs in people who have had stomach surgery, particularly BARIATRIC SURGERY for weight loss. Some research studies suggest that rapid gastric emptying in people who have not had stomach surgery may be an early sign of type 2 DIABETES. The diagnostic path may include gastroscopy and BARIUM SWALLOW to rule out other conditions. Treatment integrates dietary changes and medications to slow PERISTALSIS. Dietary changes include eating six small, low-carbohydrate meals throughout the day and drinking liquids between, rather than with, meals.

See also ENDOSCOPY.

rebound tenderness A clinical sign of PERITONITIS (generalized INFLAMMATION and INFECTION of the abdominal cavity). During abdominal palpation, the doctor presses slowly and firmly on the abdomen, then suddenly releases the pressure. The person feels a stabbing PAIN with release when the result is positive and notices no change when the result is negative. Rebound tenderness has a high level of accuracy for both positive and negative results. Rebound tenderness often appears as referred pain in appendicitis. The pressure and release action applied to the left side of the abdomen results in the person feeling pain on the right side of the abdomen, at the approximate location of the appendix.

See also DIGITAL RECTAL EXAMINATION (DRE).

rectal fistula An abnormal opening in the wall of the RECTUM, often connecting the rectum with another structure such as the URETHRA (rectourethral fistula), the VAGINA (rectovaginal fistula), or the ANUS (anorectal fistula). Rectal fistulas may be congenital or acquired. Congenital fistulas often occur in combination with other congenital anomalies, notably those affecting the HEART such as tetralogy of Fallot (a collective of malformations in the structure of the heart). Acquired rectal fistulas may be idiopathic (without detectable cause), though are more likely to occur in people who have inflammatory conditions that affect the gastrointestinal tract such as INFLAMMATORY BOWEL DISEASE (IBD). RADIATION THERAPY as treatment for PROSTATE CANCER, CERVICAL CANCER, OVARIAN CANCER, COLORECTAL CANCER, or other cancers in the abdomen can weaken the rectal wall, allowing fistulas to develop. As well, fistulas involving any portion of the gastrointestinal tract are frequent complications of HIV/AIDS.

Symptoms vary with the location of the fistula though often include FECAL INCONTINENCE or inappropriate presence of stool in the other involved structure. The diagnostic path may include DIGITAL RECTAL EXAMINATION (DRE), BARIUM ENEMA, and sigmoidoscopy (endoscopic examination of the lower COLON). Treatment is surgery to repair the fistula, which can sometimes be extensive when the fistula is long or deep. Potential complications vary according to the nature of the OPERATION necessary. In many people the surgical repairs end the symptoms and the person returns to his or her usual activities with no further problems. In some people, complications such as fecal incontinence arise or new fistulas occur.

See also ANAL FISSURE; CONGENITAL HEART DISEASE; CYSTOCELE; ENDOSCOPY; HEMORRHOIDS; ILEUS; MECONIUM; PROCTITIS; RECTOCELE.

rectal prolapse Protrusion of the rectal mucosa (lining of the RECTUM) through the ANUS. Rectal prolapse often affects women beyond MENOPAUSE who experienced trauma during vaginal CHILDBIRTH and have residual weakness of the pelvic structures. However, rectal prolapse occasionally affects men, usually those who are elderly. Long-term, chronic CONSTIPATION is a common factor when rectal prolapse occurs in women who have not given birth or in men. Prolapse of other pelvic organs, such as the BLADDER (CYSTOCELE), is also common. Rectal prolapse generally is apparent with physical examination, though the doctor often will perform sigmoidoscopy to rule out other conditions. Treatment is surgery to repair the rectal wall.

See also ENDOSCOPY; HEMORRHOIDS; ILEUS; RECTAL FISTULA; RECTOCELE.

rectocele A weakness that develops in the wall of tissue that separates the RECTUM from the VAGINA, called the rectovaginal wall, causing the rectum to protrude into the vagina. Rectocele, a type of HERNIA, most commonly appears after MENOPAUSE. Circumstances that chronically stress the muscles of the perirectal area, such as straining with bowel movements or frequent coughing due to pulmonary conditions, are frequent causes. Weakening of or damage to the perineal structures during vaginal CHILDBIRTH may also contribute to rectocele. Many women who have small rectoceles do not have symptoms. Larger rectoceles may produce symptoms that include the sensation of pressure in the vagina, pelvic PAIN, painful vaginal intercourse, and occasionally FECAL INCONTINENCE. Treatment options include KEGEL EXERCISES to strengthen the pelvic and vaginal muscles, weight loss to decrease stress on the pelvic muscles, and the insertion of a PESSARY, a fitted ring placed in the vagina to support the rectovaginal wall. Pessaries may cause irritation and INFLAMMATION, however; and women may find them uncomfortable. Surgery to repair the herniation becomes an option when other treatments fail to correct the problem and symptoms continue.

See also CYSTOCELE; PELVIC EXAMINATION; RECTAL PROLAPSE; SURGERY BENEFIT AND RISK ASSESSMENT.

rectum The segment of the COLON between the sigmoid colon and the ANUS. About six inches long, the rectum retains solid digestive waste until a BOWEL MOVEMENT expels it. The SPINAL CORD regulates the NERVE impulses that initiate the reflexive contractions of the rectum that result in bowel movements. The walls of the rectum are smooth and flexible, allowing it to expand to accommodate collected fecal material. The rectum is a frequent site of intestinal polyps and is vulnerable to CANCER. Other health conditions that can involve the rectum include ulcerative COLITIS, Crohn's disease, and DIVERTICULAR DISEASE.

COMMON CONDITIONS THAT CAN AFFECT THE RECTUM

COLITIS	COLORECTAL CANCER
CONSTIPATION	DIARRHEA
DIVERTICULAR DISEASE	FAMILIAL ADENOMATOUS POLYPOSIS (FAP)
FECAL IMPACTION	HIRSCHSPRUNG'S DISEASE
INTESTINAL POLYP	PROCTITIS
RECTAL FISTULA	RECTAL PROLAPSE
RECTOCELE	SPINAL CORD INJURY

For further discussion of the rectum and colon within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also BARIUM ENEMA; CECUM; COLONOSCOPY; COLOSTOMY; CYSTIC FIBROSIS; DIGITAL RECTAL EXAMINATION (DRE); ENDOSCOPY; ENEMA; FECAL INCONTINENCE; INTESTINAL POLYP; SMALL INTESTINE.

S

short bowel syndrome Reduction in the structural or functional length of the SMALL INTESTINE that results in MALABSORPTION, chronic DIARRHEA, and other disturbances of digestion. MALNUTRITION is a common consequence. Short bowel syndrome most often results from surgery that removes segments of the small intestine as treatment for Crohn's disease, DIVERTICULAR DISEASE, cancers of the small intestine, traumatic injury, and other conditions that irreparably damage the small intestine. Short bowel syndrome was a common complication of a weight loss operation, jejunoileal bypass, that surgeons no longer perform. Functional short bowel syndrome also may develop following severe COLITIS (such as may occur with *ESCHERICHIA COLI* O157:H7 INFECTION) or radiation GASTROENTERITIS.

Treatment options for short bowel syndrome attempt to manage symptoms such as diarrhea as well as to meet NUTRITIONAL NEEDS. Most people who develop short bowel syndrome require PARENTERAL NUTRITION, a form of long-term intravenous feeding. Surgical options include operations to extend the remaining small intestine through various procedures and SMALL BOWEL TRANSPLANTATION or multivisceral transplantation (typically small bowel and LIVER or small bowel, liver, STOMACH, and PANCREAS). The extensive presence of lymphatic tissue in the gastrointestinal tract creates IMMUNE RESPONSE challenges with transplantation.

Liver and biliary dysfunctions (notably CHOLESTASIS) are common complications of short bowel syndrome, as the JEJUNUM and ILEUM produce a number of DIGESTIVE HORMONES that help to regulate liver activity and BILE release. When these segments of the small intestine are missing or no longer functional, the body has no secondary systems to synthesize these hormones. Long-term total parenteral nutrition exacerbates liver and biliary dysfunctions. These factors tend to lead to LIVER FAILURE. Research directions for solutions to the challenges of short bowel syndrome therapies include explorations in IMMUNOTHERAPY (with a focus on suppressing the immune response in transplantation), pharmacotherapy (with a focus on supplemental hormones), and surgical methods that might improve small bowel function without transplantation.

See also CYSTIC FIBROSIS; GUT-ASSOCIATED LYMPHOID TISSUE (GALT); FOOD-BORNE ILLNESSES; INFLAMMATORY BOWEL DISEASE (IBD); MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT); RADIATION THERAPY.

sitz bath A small basin designed to accommodate the perineal and rectal areas, with the water level only to the hips. Numerous commercial products are available for ease of use at home. Placing a shallow amount of water in the regular bathtub accomplishes the same objective, which is to soothe irritated tissues caused by, for example, EPISIOTOMY incision, ANAL FISSURE, and HEMORRHOIDS. The water may contain medications or herbs for additional therapeutic effect.

See also MEDICINAL HERBS AND BOTANICALS.

small bowel transplantation Replacement of a diseased SMALL INTESTINE with a cadaver donor small intestine. Small bowel transplantation is a final treatment option for SHORT BOWEL SYNDROME or other circumstances in which there is total loss of small intestine structure or function. The gastroenterologist may consider small bowel transplantation when all other treatments, including total PARENTERAL NUTRITION, have failed. Small bowel transplantation is an extraordinarily complex procedure. The complication rate is high, and

at present the three-year success rate is about 50 percent.

The small intestine produces numerous DIGESTIVE ENZYMES and DIGESTIVE HORMONES necessary for proper function of the entire gastrointestinal tract. One challenge with small bowel transplantation is the restoration of this production. Another challenge is the abundance of lymphatic tissue in the intestinal mucosa (mucous membrane that lines the inside of the small intestine). Researchers do not yet fully understand the role of this tissue, called GUT-ASSOCIATED LYMPHOID TISSUE (GALT). However, GALT appears to intensify the IMMUNE RESPONSE typical with transplanted organs, requiring large doses of IMMUNOSUPPRESSIVE MEDICATIONS such as cyclosporine. These medications suppress immune activity throughout the body, not only in the intestinal tract, resulting in significant risk for INFECTION. Up to a third of people who receive small bowel transplantation experience complications including organ rejection and infection during the first year.

See also CYSTIC FIBROSIS; GASTROENTERITIS; ORGAN TRANSPLANTATION.

small intestine The segment of the gastrointestinal tract immediately following the STOMACH. The small intestine's three sections—DUODENUM, JEJUNUM, and ILEUM—perform about 85 percent of the digestive functions of the gastrointestinal tract. Food passes from the STOMACH to the duodenum, from the duodenum to the jejunum, and from the jejunum to the ileum. The small intestine loops and folds through the inner abdomen, with the COLON (large intestine) encircling it like a frame. Microscopic extensions, villi, arise from the mucosa, forming peaks and valleys that dramatically increase the surface area of the mucosa.

CONDITIONS THAT CAN AFFECT THE SMALL INTESTINE

BOWEL ATRESIA	CELIAC DISEASE
Crohn's disease	GASTROENTERITIS
ILEUS	LACTOSE INTOLERANCE
MALABSORPTION	PEPTIC ULCER DISEASE
WHIPPLE'S DISEASE	

A meal's transit time through the 18 or so feet of the small intestine is about 10 hours, during which intestinal mucosa (mucous membrane that lines the intestinal tract) extracts all of the nutrients, many of the electrolytes, and much of the water.

For further discussion of the small intestine within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also ANUS; FOOD-BORNE ILLNESSES; INFLAMMATORY BOWEL DISEASE (IBD); IRRITABLE BOWEL SYNDROME (IBS); RECTUM.

steatohepatitis Fatty deposits throughout the LIVER, also called fatty liver, that create irritation and INFLAMMATION. Doctors believe steatohepatitis represents a malfunction of the body's lipid processing and transfer mechanisms, many of which take place in the liver. Steatohepatitis is common with long-term ALCOHOL use and ALCOHOLISM (alcoholic steatohepatitis). It also occurs without alcohol involvement (nonalcoholic steatohepatitis), notably with DIABETES (which alters lipid METABOLISM) and OBESITY.

The most common form of steatohepatitis, called macrovesicular because the fatty deposits are large, may not show symptoms. Rather, the doctor may detect it during physical examination as HEPATOMEGALY (enlarged LIVER). When symptoms are present they reflect noninfectious HEPATITIS: JAUNDICE (yellow discoloration of the SKIN), tenderness or PAIN in the upper right abdomen, fatigue, NAUSEA, and loss of APPETITE. LIVER FUNCTION TESTS may be inconclusive; ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN often reveals the fatty accumulations. PERCUTANEOUS LIVER BIOPSY confirms the diagnosis. The form of steatohepatitis associated with alcoholism, obesity, and diabetes is macrovesicular.

Steatohepatitis occasionally manifests as an acute illness with significant symptoms and rapid progression to clotting dysfunction (coagulopathy) and neurologic involvement (hepatic NEUROPATHY). This form of steatohepatitis, called microvesicular because the fatty deposits are small, can be fatal without appropriate supportive treatment until the liver recovers.

Macrovesicular steatohepatitis generally does not require treatment though treating any underlying condition helps restore normal lipid metabolism with the result that fatty acids move out of the liver. When alcohol consumption is a factor, steatohep-

atitis nearly always goes away with abstinence from alcohol though any CIRRHOSIS (replacement of liver tissue with SCAR tissue) that has already developed is permanent. Nonalcoholic steatohepatitis associated with diabetes generally improves with tighter management of the diabetes, and with obesity when weight loss occurs. Microvesicular steatohepatitis may require extensive support, including intravenous fluids and nutrients, during its acute phase. For many people recovery is complete and without residual damage to the liver.

See also DIET AND HEALTH; LIVER DISEASE OF ALCOHOLISM.

steatorrhea Excessive excretion of fat in the stool. Steatorrheic stools are often foamy and foul-smelling, and tend to break apart and float in the toilet bowl. Steatorrhea is a symptom of numerous gastrointestinal disorders including MALABSORPTION, CELIAC DISEASE, GALLBLADDER DISEASE, PANCREATITIS, and LIVER disease. Treating the causative condition ends the steatorrhea.

See also CONSTIPATION; CYSTIC FIBROSIS; DIARRHEA.

stomach The pouchlike organ that receives and digests food. The stomach can stretch up to six times its resting size to accommodate influxes of food and drink up to about the combined quantity of a gallon. Three layers of MUSCLE wrap around the deeply pitted gastric mucosa (mucous membrane lining of the stomach). The fibers of each muscle layer run in different directions: the layer innermost to the mucosa is oblique (diagonal), the middle layer of muscle is horizontal (encircles the stomach), and the outermost layer runs lengthwise. This arrangement allows the stomach to flex and contract in every direction to mix and break apart food particles.

CONDITIONS THAT CAN AFFECT THE STOMACH

BEZOAR	Crohn's disease
CYCLIC VOMITING SYNDROME	DYSPEPSIA
GASTRITIS	GASTROESOPHAGEAL REFLUX DISORDER (GERD)
GASTROPARESIS	PEPTIC ULCER DISEASE
HIATAL HERNIA	ZOLLINGER-ELLISON SYNDROME
STOMACH CANCER	

The stomach produces gastric acid, which is primarily hydrochloric acid, and several DIGESTIVE ENZYMES. Though the stomach digests carbohydrates and some proteins, its primary role is to prepare food for the SMALL INTESTINE where the bulk of digestion takes place.

For further discussion of the stomach within the context of gastrointestinal structure and function, please see the overview section "The Gastrointestinal System."

See also COLON; DIET AND HEALTH; DIGESTIVE HORMONES; ESOPHAGUS; GASTRECTOMY; *HELICOBACTER PYLORI*; H2 ANTAGONIST (BLOCKER) MEDICATIONS; INFLAMMATORY BOWEL DISEASE (IBD); NAUSEA; NUTRITIONAL DEFICIENCY; PROTON PUMP INHIBITOR (PPI) MEDICATION; VOMITING.

stomach cancer Malignant growths that occur in the STOMACH. Stomach CANCER is seventh among deaths from cancer in the United States. About 90 percent of stomach cancers are adenocarcinomas, malignant growths that originate in the glandular cells that carpet the gastric mucosa. These are the cells that produce the stomach's acid and mucus, as well as DIGESTIVE ENZYMES. Though stomach cancer readily metastasizes (spreads) to other tissues and organs, the stomach is seldom the site of secondary cancers that originate elsewhere in the body.

Though the causes of stomach cancer remain a mystery, researchers do know certain factors alter the DNA of cells in the stomach in ways that result in the uncontrolled growth that characterizes cancer. These factors cause chronic irritation to the stomach tissues. They include

- INFECTION with *HELICOBACTER PYLORI*, believed to cause about 85 percent of PEPTIC ULCER DISEASE
- a diet high in red meats, well-done barbecued meats, and smoked meats and fish that contain nitrates or nitrites (which convert to carcinogenic substances during the digestive action of gastric juices) as preservatives
- the combination of cigarette smoking and excessive ALCOHOL consumption
- untreated or poorly controlled GASTROESOPHAGEAL REFLUX DISORDER (GERD) or Crohn's disease

Symptoms and Diagnostic Path

Symptoms of early stomach cancer are often vague and nonspecific, such as DYSPEPSIA, NAUSEA

after eating, and a sense of fullness after eating only a small amount of food. Early stomach cancers often cause microscopic bleeding that a FECAL OCCULT BLOOD TEST (FOBT) can detect. As the cancer becomes more advanced, symptoms may include

- PAIN in the upper left abdomen
- VOMITING after meals
- dyspepsia that does not go away with antacids, eating, or medications to reduce acid in the stomach
- unintended weight loss
- blood in the vomit or in the stools, which may manifest as "coffee grounds" or tarry stools
- fatigue and weakness

The diagnostic path may include BARIUM SWALLOW, upper gastrointestinal ENDOSCOPY with biopsy, and COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI). The biopsy confirms the diagnosis and identifies the kind of cancer. The pathologic examination of the tissue sample also establishes the extent to which the cancer likely has spread, called cancer staging. The cancer's stage helps determine treatment options and protocols (standards of practice), and expectations about outlook (prognosis).

Treatment Options and Outlook

The main treatment for nearly all stages of stomach cancer is surgery to remove the cancerous tumor, involved tissues, and adjacent structures such as LYMPH NODES and fatty tissue. Surgery is curative for stomach cancer detected very early (stage 0). For stage 1, 2, and 3 stomach cancers oncologists recommend CHEMOTHERAPY and RADIATION THERAPY after surgery. The chemotherapy drugs commonly used to treat stomach cancer are 5FU, cisplatin, epirubicin, and etoposide, which the oncologist may administer individually (particularly 5FU for stage 1 cancers) or in combination with one another.

The surgical options for stomach cancer include

- endoscopic resection, in which the surgeon removes the tumor and a safe margin of stomach tissue endoscopically

BASIC STAGING OF STOMACH CANCER

Stage	Meaning	Treatment Protocol
stage 0	CANCER is in its earliest stages, completely confined to the gastric epithelium (lining of the STOMACH); also called CARCINOMA in situ	endoscopic resection, partial GASTRECTOMY, or total gastrectomy to remove the cancerous tumor
stage 1	cancer involves the gastric mucosa but remains confined to the stomach	partial or total gastrectomy with removal of adjacent fatty tissue and lymph nodes
stage 2	cancer extends into and beyond the MUSCLE layers of the stomach and may involve up to 15 adjacent LYMPH NODES	partial or total gastrectomy with extensive removal of adjacent fatty tissue and lymph nodes RADIATION THERAPY or CHEMOTHERAPY; occasionally a combination of both
stage 3	cancer extends beyond the stomach into adjacent lymph nodes and nearby organs such as the SPLEEN, LIVER, PANCREAS, or intestine	total gastrectomy with extensive removal of adjacent fatty tissue and lymph nodes surgery to remove tumors in other organs radiation therapy and chemotherapy
stage 4	cancer has spread from the stomach to other organs throughout the body	palliative surgery, chemotherapy, or radiation therapy to relieve symptoms, obstruction, and bleeding that may occur

- partial GASTRECTOMY, in which the surgeon removes the section of stomach containing the tumor
- total gastrectomy, in which the surgeon removes the entire stomach and an area of surrounding adipose (fatty) tissue called the omentum
- lymphadenectomy, in which the surgeon removes the adjacent lymph nodes

Few lifestyle modifications beyond those to decrease the risk for recurrent or other cancers, are necessary for people who have endoscopic resections. Partial gastrectomy requires moderate changes in diet and EATING HABITS to accommodate the reduced size of the stomach, primarily a shift to eating smaller meals more frequently and reducing the amount of carbohydrates in the diet. Total gastrectomy requires significant modifications in eating habits as the surgery connects the lower end of the ESOPHAGUS to the start of the DUODENUM, leaving no reservoir for ingested food. Most people can eat only a few bites of food at a time after total gastrectomy, making eating enough to meet the body's nutritional needs a fairly continuous process. As well, because the stomach produces the substances that make it possible for the body to absorb vitamins such as vitamin B_{12}, people who undergo total gastrectomy need NUTRITIONAL SUPPLEMENTS.

The outlook for stage 0 stomach cancer is excellent, with a 90 percent of people who undergo surgery reaching the five-year survival mark. The outlook remains very good for stage 1 stomach cancer, with about a 70 percent five-year survival rate. More advanced stages of stomach cancer, in which the cancer spreads to involve other tissues and organs, remain difficult to treat successfully. Clinical research studies may offer the opportunity to participate in investigational treatments that extend life as well as improve QUALITY OF LIFE.

Risk Factors and Preventive Measures

As is the case with many kinds of cancer, age is the most significant risk factor. Most stomach cancers occur in people over age 60. Family history of stomach cancer or COLORECTAL CANCER (which is also an ADENOCARCINOMA of the gastrointestinal tract), long-term cigarette smoking (particularly in combination with excessive alcohol consumption) and OBESITY also raise the risk for stomach cancer. The most valuable preventive measure is FOBT to screen for the presence of blood in the gastrointestinal tract. Bleeding raises suspicion for several kinds of cancer that are highly treatable with early detection and intervention. People who have peptic ulcer disease should be tested and treated for *H. pylori* infection. A diet high in vegetables and low in smoked or preserved foods seems to lower the risk for stomach cancer.

See also ADENOCARCINOMA; ADENOMA-TO-ADENOCARCINOMA TRANSITION; CANCER RISK FACTORS; CANCER PREVENTION; CANCER TREATMENT OPTIONS AND DECISIONS; END OF LIFE CONCERNS; INFLAMMATORY BOWEL DISEASE (IBD); INTESTINAL POLYP; LIVER CANCER; LYMPHEDEMA; PANCREATIC CANCER; SMOKING AND CANCER; STAGING AND GRADING OF CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

T–Z

toxic megacolon A serious condition in which a loss of MUSCLE tone in the lower COLON (typically the sigmoid colon) causes the preceding segment of colon to greatly enlarge (dilate). Air accumulates in the dilated bowel, increasing the pressure. Without prompt treatment intestinal perforation (rupture) is highly likely, with consequential PERITONITIS.

Toxic megacolon is a potentially life-threatening condition that requires emergency medical treatment and often surgery.

Toxic megacolon is usually a complication of inflammatory conditions affecting the gastrointestinal tract, such as INFLAMMATORY BOWEL DISEASE (IBD) or INFECTION (COLITIS). The congenital disorder HIRSCHSPRUNG'S DISEASE, in which the lower colon lacks nerves, can cause toxic megacolon in a newborn infant.

Symptoms and Diagnostic Path

A person who has toxic megacolon is very sick. Usually there is FEVER along with ABDOMINAL DISTENTION, rigidity, and PAIN. REBOUND TENDERNESS and absence of BOWEL SOUNDS are common findings. The person may be in SEPTICEMIA (septic SHOCK), indicating PERITONITIS. The doctor often can make the diagnosis with an abdominal X-RAY that shows the dilated colon.

Treatment Options and Outlook

ANTIBIOTIC MEDICATIONS, CORTICOSTEROID MEDICATIONS, depending on the cause of the condition, and intravenous fluids to counter DEHYDRATION may help stabilize the colon, in combination with positional changes to attempt to move air (intestinal gas) out of the bowel to help relieve the distention. Surgery to remove the dilated segment of bowel (colectomy) is often the only treatment to prevent or treat bowel perforation. The surgeon then connects the two healthy ends of bowel together to restore normal bowel function. With prompt and appropriate treatment, many people make a full recovery from toxic megacolon. However, it does present a serious challenge to the body's HEALING abilities. As well, any underlying conditions that precipitated the bowel dilation may continue to cause symptoms.

Risk Factors and Preventive Measures

The primary risk factor for toxic megacolon is any condition that causes INFLAMMATION of the colon. Taking medications to slow gastric motility (such as to treat DIARRHEA) may contribute to the circumstances resulting in toxic megacolon. Anyone who has colitis, GASTROENTERITIS, DIVERTICULAR DISEASE, CELIAC DISEASE, IBD, or other inflammatory condition affecting the gastrointestinal tract who experiences symptoms that could suggest toxic megacolon should see a doctor without delay.

See also ILEUS; SHORT BOWEL SYNDROME.

tube feeding See ENTERAL NUTRITION.

ulcer See PEPTIC ULCER DISEASE.

ulcerative colitis See INFLAMMATORY BOWEL DISEASE (IBD).

virtual colonoscopy See COLONOSCOPY.

vomiting The forceful expulsion of contents from the STOMACH, also called emesis. The force of vomiting may also draw digestive material from

the DUODENUM (first section of the SMALL INTESTINE). Like sneezing and coughing, vomiting is a protective and reflexive mechanism to rid the body of substances that threaten its well-being.

Vomiting occurs in response to NERVE impulses from the BRAIN's emesis center (also called vomiting center). The emesis center receives input from numerous body systems, including the gastrointestinal tract, vestibular system (which regulates balance), and circulatory system, as well as from the chemoreceptor trigger zone, another region of the brain that receives signals from the body. PAIN signals, particularly those the vagus nerve conveys, also travel to the emesis center, which is why severe pain may result in NAUSEA (queasiness and the feeling of being about to vomit) and vomiting.

Other variables that influence the emesis center include sensory perceptions such as foul smells or disturbing sights (which activate the chemoreceptor zone), hormonal shifts (such as occur in pregnancy to cause MORNING SICKNESS), and signals from the gastrointestinal tract indicating chemical changes such as from the presence of INFECTION or INFLAMMATION. Nausea, the sensation of queasiness and the urge to vomit, typically though not always precedes vomiting.

A complex series of physiologic events takes place to permit vomiting. Simultaneously the epiglottis closes (blocking the airway), the larynx lifts, and the upper esophageal sphincter opens. Then the DIAPHRAGM violently contracts, pulling it down and causing the open the lower esophageal sphincter to open, while the abdominal muscles contract with comparable force to push gastric (stomach) contents upward through the now open esophagus. Vomitus is highly acidic; chronic vomiting such as occurs with anorexia nervosa causes erosion of the tooth enamel. This material has a bitter taste and often leaves a burning sensation in the upper THROAT. Though the mechanism of vomiting is involuntary, there is some voluntary control over its initiation.

Episodic vomiting generally has no lasting consequences, though the very young and the very old can quickly become dehydrated. Vomiting that continues longer than three or four weeks without apparent cause requires medical evaluation. Treatment may include ANTIEMETIC MEDICATIONS, dietary changes, or therapies to resolve underlying conditions. Complications of chronic or repeated vomiting may include ESOPHAGITIS, electrolyte imbalance, and ASPIRATION PNEUMONIA.

See also COUGH; CYCLIC VOMITING SYNDROME; DEHYDRATION; EATING DISORDERS; FOOD-BORNE ILLNESSES; LABYRINTHITIS; MÉNIÈRE'S DISEASE; SNEEZE.

Whipple's disease A bacterial INFECTION of the SMALL INTESTINE, also called intestinal lipodystrophy, that impairs absorption of fats (lipids). The PATHOGEN (infective BACTERIA) is *Tropheryma whippelii*. Though *T. whippelii* can infect various body systems including the HEART and the EYE, the gastrointestinal tract is its most common site. In the small intestine the bacteria create lesions (disruptions in the continuity of the intestinal mucosa) that destroy the villi, the microscopic, fingerlike extensions of tissue where much of the intestine's absorption functions take place. Researchers do not know how people acquire *T. whippelii*, though do know the infection can take years to decades to manifest symptoms.

Symptoms include DIARRHEA, GASTROINTESTINAL BLEEDING, OSTEOARTHRITIS, MALNUTRITION, unintended weight loss, HEADACHE, and FEVER. The diagnostic path may include general blood tests, BARIUM SWALLOW with small intestine flow-through, and ENDOSCOPY with biopsy to culture a tissue sample from the inner intestine. Treatment is a course of intravenous ANTIBIOTIC MEDICATIONS, typically penicillin and streptomycin or chloramphenicol in combination, with 12 to 18 months of oral antibiotic therapy to completely eradicate the bacteria.

See also GASTROENTERITIS; MALABSORPTION.

Zollinger-Ellison syndrome A rare disorder in which the STOMACH dramatically increases hydrochloric acid production, resulting in rampant PEPTIC ULCER DISEASE. Zollinger-Ellison syndrome develops as a consequence of benign tumors, called gastrinomas, that secrete the digestive HORMONE gastrin. Gastrin signals the stomach to produce acid, which the stomach continues doing as long as gastrin remains present. The excess acid that results causes extreme irritation of the gastric mucosa (stomach's lining), leading to numerous ulcers. The gastrinomas may form in the PANCREAS or the DUODENUM (first segment of SMALL INTESTINE).

Though gastrinomas are noncancerous, they often spread to other locations (notably the LIVER) and may develop into CANCER over time. Doctors do not know what causes Zollinger-Ellison syndrome though it appears to have a correlation with MULTIPLE ENDOCRINE NEOPLASIA (MEN) type 1, a disorder in which tumors (including gastrinomas) develop in numerous endocrine glands.

The symptoms of Zollinger-Ellison syndrome are the same as those for peptic ulcer disease (DYSPEPSIA, NAUSEA, sensation of fullness, possible GASTROINTESTINAL BLEEDING). ENDOSCOPY of the upper gastrointestinal tract may reveal gastrinomas in the duodenum. Abdominal ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI) can detect gastrinomas in the pancreas or the duodenum. Treatment combines medication to reduce gastric acid production, such as H2 ANTAGONIST (BLOCKER) MEDICATIONS or PROTON PUMP INHIBITOR (PPI) MEDICATIONS, and surgery to remove or reduce the gastrinomas when possible.

See also CANCER RISK FACTORS; CANCER PREVENTION; LIVER CANCER; PANCREATIC CANCER; PANCREATITIS; STOMACH CANCER.

THE ENDOCRINE SYSTEM

The endocrine glands produce hormones, chemical messengers that regulate many functions within the body. Physician specialists who treat endocrine conditions are endocrinologists and neuroendocrinologists. This section, "The Endocrine System," presents a discussion of the endocrine glands and other structures, the hormones they produce and their functions, an overview of endocrine health and disorders, and entries about the health conditions that involve the endocrine system.

Structures of the Endocrine System

HYPOTHALAMUS
PITUITARY GLAND
- anterior pituitary lobe
- posterior pituitary lobe

PINEAL GLAND
THYROID GLAND
PARATHYROID GLANDS
THYMUS
ISLETS OF LANGERHANS
ADRENAL GLANDS
- adrenal cortex
- adrenal medulla

OVARIES (female)
TESTICLES (male)

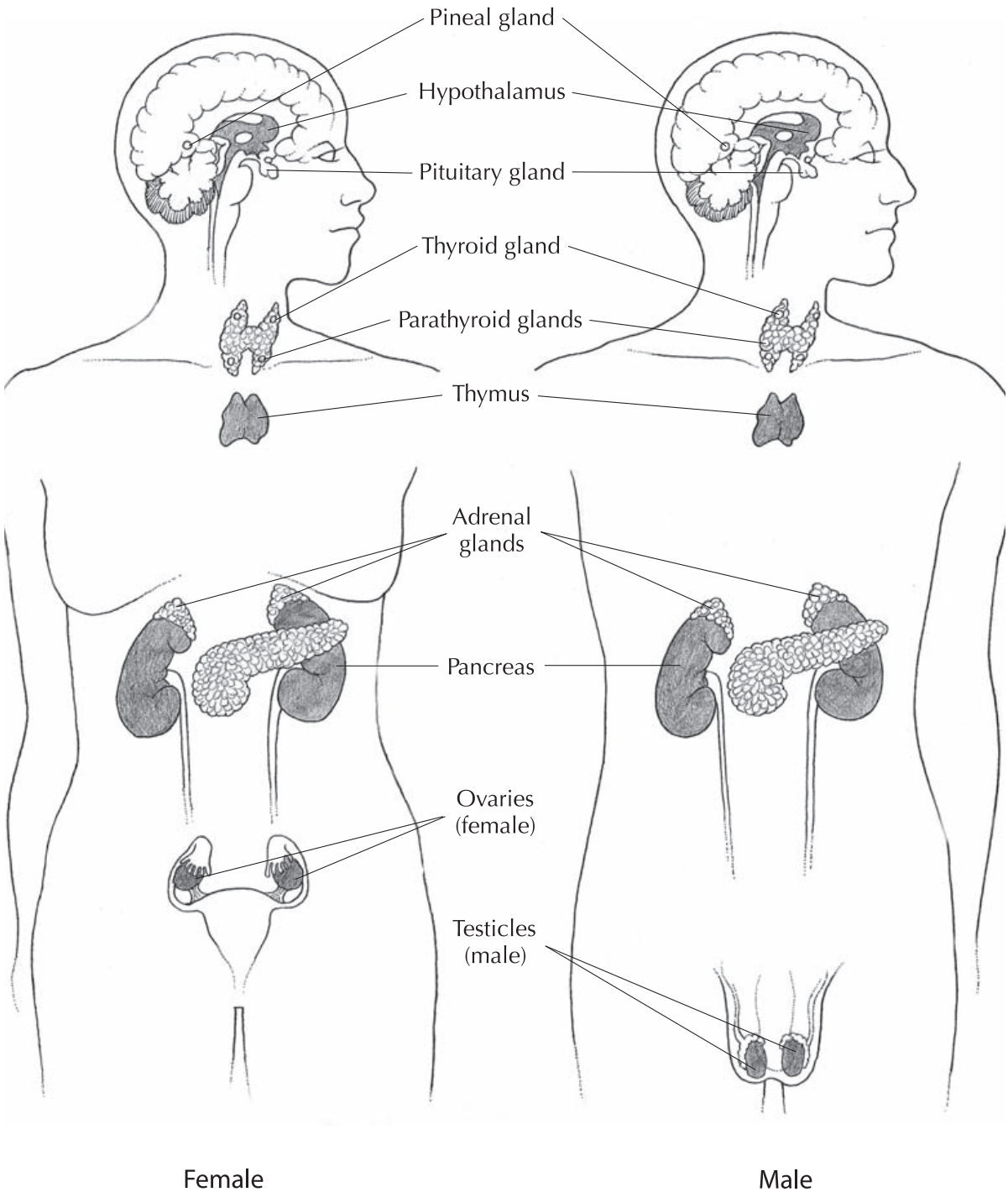
Functions of the Endocrine System

The endocrine system and the NERVOUS SYSTEM work in tandem to direct and regulate the myriad functions of the body, the nervous system through electrical impulses that travel along the nerves and the endocrine system via chemical messengers called hormones. Endocrine glands, sometimes called ductless glands, produce hormones. The endocrine glands release their hormones directly into the bloodstream, and the bloodstream transports them to the cells. Cells throughout the body contain receptors for specific hormones, so even though hormones circulate freely through the blood they affect the functions of only the cells that have receptors for them.

The endocrine glands may be clearly defined or loosely configured structures and are in numerous locations throughout the body. Some collections of endocrine cells inhabit other tissues and organs, such as those in the STOMACH and SMALL INTESTINE, and in the ISLETS OF LANGERHANS in the PANCREAS. Other endocrine cells form organized and independent structures, such as the ADRENAL GLANDS that cap the KIDNEYS and the THYROID GLAND which lies across the front of the THROAT. Each endocrine structure produces specific hormones. Collectively the endocrine structures function in intimate synchronization and interaction with each other, continuously adjusting their secretions to accommodate the ever-changing conditions and needs of the body. An intricate matrix of cascades and feedback mechanisms allows this dynamic coordination to initiate and inhibit cellular activity.

THE MAJOR ENDOCRINE STRUCTURES AND THEIR HORMONES

Endocrine Structure	Primary Hormones
ADRENAL GLANDS	
adrenal cortex	ALDOSTERONE
	CORTISOL
	DEHYDROEPIANDROSTERONE (DHEA)
adrenal medulla	DOPAMINE
	EPINEPHRINE
	NOREPINEPHRINE
gastrointestinal tract	cholecystokinin (CCK)
	enterogastrone
	gastric inhibitive polypeptide (GPI)
	gastrin
	motilin
	secretin
	SOMATOSTATIN
	vasoactive intestinal peptide (VIP)
HYPOTHALAMUS	ANTIDIURETIC HORMONE (ADH)
	CORTICOTROPIN-RELEASING HORMONE (CRH)


Pineal gland
Hypothalamus
Pituitary gland
Thyroid gland
Parathyroid glands
Thymus
Adrenal glands
Pancreas
Ovaries (female)
Testicles (male)
Female
Male

Endocrine Structure	Primary Hormones
HYPOTHALAMUS (continued)	dopamine
	GONADOTROPIN-RELEASING HORMONE (GNRH)
	GROWTH HORMONE-RELEASING HORMONE (GHRH)
	OXYTOCIN
	somatostatin
	THYROTROPIN-RELEASING HORMONE (TRH)
ISLETS OF LANGERHANS	GLUCAGON
	INSULIN
	somatostatin
KIDNEYS	ERYTHROPOIETIN (EPO)
	RENIN
ovaries	ESTROGENS
	INHIBIN
	PROGESTERONE
PARATHYROID GLANDS	PARATHYROID HORMONE
PINEAL GLAND	MELATONIN
PITUITARY GLAND	
anterior pituitary lobe	ADRENOCORTICOTROPIN HORMONE (ACTH)
	FOLLICLE-STIMULATING HORMONE (FSH)
	GROWTH HORMONE (GH)
	LUTEINIZING HORMONE (LH)
	PROLACTIN
	THYROID-STIMULATING HORMONE (TSH)
posterior pituitary lobe	stores and releases as needed: ADH
	oxytocin
PLACENTA	CHORIONIC GONADOTROPIN
	estrogen
	prolactin
	human placental lactogen (hPL)
	progesterone
	RELAXIN
testes	inhibin
	TESTOSTERONE
THYMUS	THYMOSIN
THYROID GLAND	CALCITONIN
	THYROXINE (T_4)
	TRIIODOTHYRONINE (T_3)

Bridge between control systems: the hypothalamus The HYPOTHALAMUS is the structural and functional bridge between the BRAIN and the endocrine system. Composed primarily of brain tissue, it receives a constant barrage of NERVE signals from the thalamus, a structure of the brain that serves as a neurologic switchboard for sensory information related to sight, sound, touch, and taste. The physical transition from thalamus to hypothalamus is difficult to distinguish, highlighting the blurred line between neurologic and endocrine activity that gives rise to the subspecialty of medicine known as neuroendocrinology.

The functions of the hypothalamus primarily relate to survival. Through a combination of nerve impulses and hormonal signals, the hypothalamus regulates BLOOD PRESSURE, HEART RATE, gastrointestinal activity and digestion, body temperature, hunger, and thirst. Hypothalamic hormones target the PITUITARY GLAND, acting either to stimulate or inhibit (stop) the pituitary's secretions. The hypothalamus receives hormonal messages directly from the pituitary gland and indirectly through HORMONE levels in the BLOOD, one of a number of feedback mechanisms that helps regulate the hypothalamus's hormonal activity and maintain hormonal balance within the body.

Hormonal choreography: the pituitary gland Extending downward from the base of the hypothalamus, the pituitary gland bulbs out from the end of a short stalk. A dedicated capillary network, the hypophyseoportal circulation, circulates blood between the hypothalamus and the pituitary gland to fast track hormone delivery from the hypothalamus to the pituitary gland. A separate network of blood vessels supplies each structure with blood from the body's circulation to meet the metabolic needs of its cells and to carry pituitary hormones into the body. Communication between the pituitary gland and the hypothalamus is by necessity intimate and continuous, as the relationship between these two structures regulates basic bodily functions of survival.

The pituitary gland has two structural and functional divisions: the anterior lobe and the posterior lobe. The anterior pituitary lobe directs the activities of the thyroid, parathyroid, adrenal, and sex glands (gonads). The posterior pituitary lobe stores and secretes two hormones it receives from the hypothalamus: ANTIDIURETIC HORMONE (ADH), sometimes called vasopressin, and OXYTOCIN. The release of ADH directs the KIDNEYS to withhold more water, increasing blood volume and thus blood pressure. Oxytocin stimulates contractions of the UTERUS during CHILDBIRTH, and the mother's letdown REFLEX when BREASTFEEDING. Oxytocin also appears to play a role in sexual arousal in both women and men.

Recent research suggests oxytocin interacts with the limbic system, the intersection of neurologic and biochemical response to emotional stress. Levels of oxytocin in the bloodstream rise when stress hormone levels rise, leading researchers to speculate that oxytocin presents a counterbalance to the fight-or-flight response the stress hormones evoke by helping calm the body and restore homeostasis.

Stress management: the adrenal glands The adrenal glands drape across the tops of the kidneys. They produce an array of hormones that increase body functions in response to physiologic stress, such as heart rate and blood pressure. The two portions of the adrenal gland—the cortex (outer portion) and the medulla (inner portion)—have unique functions. The adrenal cortex, rindlike in appearance, secretes steroid hormones that it synthesizes from cholesterol. The primary adrenal cortex hormones are ALDOSTERONE and CORTISOL. Aldosterone regulates the fluid balance in the blood by directing the absorption of water and sodium in the kidneys. This is a fundamental component of a blood pressure–regulation mechanism called the RENIN-angiotensin-aldosterone (RAA) system. Cortisol has numerous effects related to metabolic functions throughout the body. The adrenal cortex also produces small amounts of estrogen, PROGESTERONE, and TESTOSTERONE in men and women alike.

The adrenal medulla, the core of the adrenal gland, secretes EPINEPHRINE, NOREPINEPHRINE (also called adrenaline and noradrenaline), and DOPAMINE. These hormones initiate rapid increases in heart rate, respiration, and blood pressure, along with changes blood distribution, to allow the body to enter the classic fight-or-flight mode—the stress response. These hormones also provide the "adrenaline rush" that appeals to people who enjoy high-risk activities. Chemically these three substances are catecholamines. In the bloodstream the catecholamines are hormones regulating cell activity. In the interstitial (between-cell) fluid, they function as neurotransmitters, facilitating electrical impulses between nerves. The midbrain, including the hypothalamus, controls the adrenal medulla's secretory activity.

DOPAMINE "TRANSPLANT" FOR PARKINSON'S DISEASE

In the 1980s neurologists experimented with transplanting adrenal medullary tissue into the brains of people who had PARKINSON'S DISEASE, a progressively degenerative condition that results from depleted DOPAMINE in the BRAIN. Doctors hoped the adrenal medullary tissue would take root in the brain and continue to produce NOREPINEPHRINE, a precursor HORMONE to dopamine, which other brain chemicals would convert to much-needed dopamine. The risks of the procedure far outweighed the possible benefits, however, and failed to produce consistent results. Doctors today have largely abandoned the method.

Metabolic homeostasis: the thyroid gland Spread across the throat like an elongated butterfly, the thyroid gland secretes the hormones THYROXINE (T_4) and TRIIODOTHYRONINE (T_3), which direct the rate at which cells consume energy. These hormones regulate numerous body functions, notably heart rate, digestive rate, and thermoregulation (body temperature, particularly response to cold). The thyroid's two lobes perform the same functions. The thyroid gland also secretes CALCITONIN, which acts to decrease calcium levels in the blood.

Thyroid hormones are essential for life. People who have HYPOTHYROIDISM (underactive thyroid gland) or who have had their thyroid glands destroyed or surgically removed must take lifelong thyroid hormone supplement or replacement therapy. Congenital thyroid deficiency, once called cretinism, in which the thyroid gland is missing or

dysfunctional in the unborn child, results in permanent damage to growth, development, and intellect. HYPERTHYROIDISM, in which the thyroid gland secretes excessive thyroid hormones, can cause serious and permanent damage to the HEART and to the eyes (GRAVES'S OPHTHALMOPATHY).

Calcium balance: the parathyroid glands Arising from the surface of the thyroid gland where it wraps around the TRACHEA are the four tiny PARATHYROID GLANDS, arranged in pairs on each of the thyroid gland's two lobes. Though each parathyroid gland alone is barely the size of a grain of rice, the parathyroid glands collectively keep the heart beating, the muscles moving, and the bones solid. The parathyroid glands produce PARATHYROID HORMONE, also called parathormone, which regulates the balance between calcium and phosphate. This equilibrium is essential for the conduction of nerve impulses in the heart and the skeletal muscles, proper growth of the bones and TEETH in childhood, and BONE DENSITY and STRENGTH in adulthood. The relationship between the thyroid gland and the parathyroid glands is functionally as well as physically intimate. The release of parathyroid hormone causes calcium levels in the blood to rise, counterbalancing the actions of calcitonin.

Glucose balance: the islets of Langerhans Distributed throughout the exocrine cells that make up the pancreas are about a million clusters of endocrine cells ranging in size from a few dozen to a few hundred cells. These clusters are the islets of Langerhans, and their three distinct cell types secrete the hormones GLUCAGON, INSULIN, and SOMATOSTATIN. These hormones regulate the body's balance and use of GLUCOSE, the primary source of fuel for many functions of METABOLISM. The islet cells also secrete a number of other hormones whose functions remain less clearly understood.

Reproduction: the gonads (sex glands) The gonads (sex glands)—the OVARIES in women and the testes in men—produce the hormones responsible for sexual maturity and reproductive capability. The gonads become active at PUBERTY, when the hypothalamus signals the pituitary gland to begin producing FOLLICLE-STIMULATING HORMONE (FSH) and LUTEINIZING HORMONE (LH). These hormones in turn stimulate the gonads to produce the sex hormones. Men and women alike have all of these hormones in their bodies; men have a predominance of testosterone and women have a predominance of estrogen and progesterone.

In women the ovaries produce estrogen, progesterone, and a small amount of testosterone. In men the testes produce testosterone, INHIBIN (which regulates SPERM production), and a small amount of estrogen along with a number of other minor hormones that have narrowly specialized functions. In men and women alike, the adrenal cortex produces small amounts of estrogen, progesterone, and testosterone. Estrogen is important for lipid metabolism and storage, testosterone is important for building and maintaining MUSCLE mass, and progesterone is an important precursor hormone for the synthesis of other steroid (lipid-based) hormones.

Building the immune system: the thymus In the 1940s doctors believed there was a connection between an enlarged THYMUS and sudden, unexplainable death in infants. They termed this condition status thymicolymphaticus and treated it with RADIATION THERAPY to destroy the thymus. There was little evidence to support this connection, however, and doctors began to notice that children treated with irradiation were unusually susceptible to infection. By the 1960s, as understanding began to grow about the functions of the immune system and researchers began to recognize the thymus had a role in immune function, and doctors abandoned both the concept of status thymicolymphaticus and its treatment.

The thymus secretes the hormone THYMOSIN, which helps the immune system's T-cell lymphocytes reach maturity and stimulates blood stem cell production in the BONE MARROW. Researchers speculate the thymus also produces several as yet unidentified hormones that influence immune function. Doctors now know, too, that the normal release of GROWTH HORMONE (GH) during the middle years of childhood stimulates an increase in the size of the thymus, explaining the reason for its enlargement in young children. During this period of development the thymus becomes particularly active in maturing and releasing into the body the T-cells that will form the foundation of immune function for the remainder of life.

Circadian cycles: the pineal gland The PINEAL GLAND, a small pinecone-shaped structure buried

deep in the brain, releases MELATONIN, a hormone associated with sleep cycles. Eastern traditions have long viewed the pineal gland as the metaphysical "third eye," an energy pathway by which the brain communicates directly with the external environment. Western researchers are now discovering this perception may have tangible scientific substance. The pineal gland is located near the optic nerve, which appears to convey input about external light and dark to the pineal gland. Though researchers do not yet fully understand the mechanisms through which this occurs, they do know that melatonin secretion increases with darkness and decreases with lightness, apparently to facilitate the circadian cycle of sleep and wakefulness. Though as yet melatonin is the only identified hormone the pineal gland produces, researchers believe the pineal gland has additional functions and continue to study its role in the body.

Hormonal rhythms, cascades, and feedback loops The structures of the endocrine system function in tight synchronization with one another. Some hormonal processes are cyclic, under the control of the body's circadian rhythm. Others are "on demand," with physiologic events triggering the release of hormones.

For example, the hypothalamus releases CORTICOTROPIN-RELEASING HORMONE (CRH) on a regular cycle that begins a sharp spike a few hours before daybreak and peaks a few hours later, dropping off over the daylight hours to trough in the early evening. The release of CRH initiates a cascade of hormonal responses that accelerate metabolism in preparation for the body's heightened level of activity during waking hours: CRH stimulates the pituitary gland to release ADRENOCORTICOTROPIC HORMONE (ACTH), which subsequently stimulates the adrenal cortex to release cortisol. Cortisol then initiates numerous metabolic actions throughout the body.

Correspondingly, hormonal activity from the thyroid gland, islets of Langerhans, and gastrointestinal tract accelerates, instigating further cascades of hypothalamic-pituitary-adrenal activity. As the flow of CRH diminishes, the hormonal cascade slows. Feedback mechanisms also come into play. Cortisol reaches a certain level in the blood circulation, signaling the hypothalamus to stop releasing CRH. The body's metabolic activity begins to drop off. By nightfall the CRH level reaches its lowest point, and the body is metabolically ready for rest. The pineal gland's release of melatonin similarly follows, and may in fact establish, the body's circadian rhythm.

Other hormonal cycles follow different patterns. The hormonal cascades of puberty, for example, continue during the period of growth during which the secondary sex characteristics emerge—typically a range between the ages of 11 to 12 and 18 to 20. A woman's MENSTRUAL CYCLE repeats approximately every 28 days. The hormones of PREGNANCY follow a precise schedule. Additional hormonal activity occurs in response to physiologic needs in integration with routine hormonal cycles. Feedback loops regulate such activity, with the endocrine system responding to stimuli from other body systems.

During intense physical exercise, for example, the hypothalamus releases ADH in response to hormonal signals from the kidneys (renin release) and barosensory signals from the cardiovascular system, stimulating the adrenal glands to release aldosterone, epinephrine, and norepinephrine to readjust fluid volume, electrolyte balance, heart rate, BREATHING rate, and blood pressure. The various physiologic changes that occur then signal the hypothalamus to stop releasing ADH. Such changes may take the form of rising levels of hormones in the blood or events that indicate the body's needs are being met, such as increased blood volume and elevated blood pressure. Some hormones, such as ADH, are stimulatory; they initiate activity. Other hormones, such as somatostatin, are inhibitory; they stop activity.

Health and Disorders of the Endocrine System

Some endocrine structures are more active early in life, then recede to maintenance roles later in life. The thymus, for example, establishes the foundation of the immune system in early to middle childhood and subsequently shrinks in size and function at puberty to take a background, supportive role in immune function. Other endocrine structures become active at puberty such as the ovaries (female) or testes (male), known collectively as the gonads or sex glands. The sex glands establish the body's SECONDARY SEX-

UAL CHARACTERISTICS and reproductive maturity. The functions of the sex glands taper with aging, most prominently in women to define the conclusion of FERTILITY (MENOPAUSE). Though men can remain fertile throughout their lives, testosterone levels begin to gradually diminish in the mid-30s. Still other endocrine tissues function only under special circumstances, such as the PLACENTA which secretes dozens of hormones that regulate pregnancy.

The most common endocrine disorder in the United States is DIABETES (known clinically as diabetes mellitus). Approximately 13 million Americans know they have diabetes, and health experts believe another 5 to 6 million more have diabetes though do not yet know, more than half of whom are over age 60. Diabetes is a significant health influence among adults as the leading cause of heart disease, kidney disease, blindness, and nerve damage (NEUROPATHY). Diabetes accounts directly for more than 70,000 lives lost each year, making it the sixth leading cause of death in the United States. Some people are able to manage their diabetes through lifestyle factors such as diet, exercise, and WEIGHT LOSS AND WEIGHT MANAGEMENT. Others must take medication such as oral antidiabetic medications or insulin injections. Type 1 diabetes is an autoimmune disorder in which the immune system attacks the islets of Langerhans, killing the cells that produce insulin. Type 2 diabetes typically develops in midlife or later, nearly always as a consequence of INSULIN RESISTANCE arising from lifestyle factors. Health experts believe most type 2 diabetes is preventable.

Also common is hypothyroidism (underactive thyroid). About 5 million Americans know they have hypothyroidism. Hypothyroidism affects numerous body functions, including heat regulation, heart rate, blood pressure, body weight, fertility, energy levels, and sleep quality. As with diabetes, health experts believe many more—perhaps another 10 million—have the condition and do not yet know. Hypothyroidism is more common among women and becomes more frequent with advancing age, with some health experts estimating as many as 20 percent of women over age 60 have the condition.

OBESITY, in which body weight due to excessive body fat is 20 percent or more greater than healthy weight, is a complex confluence of endocrine, genetic, and lifestyle factors. Much research focuses on the role of hormones in body functions related to APPETITE (the desire to eat) and metabolism. Research in the 1990s identified two hormones, leptin and ghrelin, that strongly influence appetite. The stomach secretes ghrelin, and adipose (fat) cells throughout the body secrete leptin. The hypothalamus perceives the changing levels of these hormones in the bloodstream as signals of either hunger or satiety (sense of fullness), and correspondingly accelerates or decelerates digestion and metabolism (use of energy). This research holds intriguing implications, especially for type 2 diabetes. Doctors know that 90 percent of people who have type 2 diabetes also have obesity and estimate that a comparable percentage of people who have obesity also have either insulin resistance or diabetes. Health experts estimate obesity affects 15 percent of American children and 30 percent of American adults.

Traditions in Medical History

For centuries mystery shrouded the very existence of the endocrine glands and their functions. Until human autopsy (cutting open the body after death) became ethically and legally acceptable, doctors learned of endocrine glands or their functions only unintentionally. Physicians knew the signs consistent with the diseases of endocrine dysfunction but lacked the understanding of their causes and thus could not treat them. Historical records dating from ancient Mesopotamia, India, Greece, Rome, and China, for example, document the universal manifestation of diabetes, the first recognized, and even today the most common, endocrine disorder. In diabetes, the islets of Langerhans, collections of endocrine cells in the pancreas, stop secreting insulin, the hormone that "unlocks" cells to allow glucose (sugar), their primary fuel, to enter. As a result, glucose accumulates in the blood while cells literally starve to death.

Antiquarian healers diagnosed diabetes using the same concept modern doctors use (though with vastly different methods), testing the URINE for sugar. Because blood glucose levels rise with inadequate insulin presence, the kidneys attempt to restore the balance by extracting glucose from

the blood and passing it into the urine for excretion from the body. Though the modern method employs laboratory equipment that measures the amount of glucose present in the urine, the ancient physician relied on a far less sophisticated approach: An unfortunate assistant tasted the patient's urine, with sweetness confirming the diagnosis. More innovative or perhaps simply less influential healers had their patients urinate on the ground, then watched to see whether ants swarmed to the site. When ants were attracted to the urine, the diagnosis was "honey urine disease," known today as diabetes.

The diagnosis unfortunately offered little hope for treatment. Ancient healers knew honey urine was a harbinger of death but they did not understand the accountable disease mechanisms. Not until the early 20th century did the scientists Frederick Banting (1891–1941), Charles Best (1899–1978), and John James Rickard Macleod (1876–1935) discover insulin and correlate it to pancreatic function and diabetes. Their research ultimately demonstrated that regular injections of a purified solution prepared with ground pancreatic tissue from pigs or cows, which provided insulin, restored glucose metabolism in people who had diabetes.

The work earned the trio the 1923 Nobel Prize in Physiology or Medicine. More significant, it gave the prospect of normal life to countless people otherwise consigned to near-certain death. And it threw open the door to expanded knowledge of the role of the body's chemical messengers in health and in illness. Modern researchers hope to build on this knowledge to find a cure for diabetes, a disorder that despite treatment remains the leading cause of RENAL FAILURE and blindness and a significant cause of CARDIOVASCULAR DISEASE (CVD).

Breakthrough Research and Treatment Advances

The 20th century saw the field of endocrinology grow from the introduction of the term *hormone* in 1902 to amazing breakthroughs in understanding of, and treatments for disorders of, endocrine function and neuroendocrine interactions. Researchers now know of nearly 100 hormones the body produces and have developed synthetic hormones to replace or supplement the body's natural hormones as treatments for conditions such as diabetes, hypothyroidism, and osteoporosis. People who have insulin-dependent diabetes now take injections of insulin products genetically engineered in the laboratory to emulate human insulin's precise molecular structure, no longer dependent on purified extracts from animal tissues. Research exploring ISLET CELL TRANSPLANTATION shows promise for being among the therapies that might someday allow doctors to cure diabetes.

Researchers entered other frontiers of endocrine understanding as well. In 1935 scientists finally isolated and named testosterone, the male sex hormone. Shortly after came the discovery of estrogen, the female sex hormone. A quarter century later researchers had turned this knowledge into significant advances on both ends of the fertility spectrum, with the debut of the oral contraceptive (birth control pill) in 1960 and the birth of the first "test tube baby" in 1978. Both discoveries manipulate the hormones responsible for OVULATION, CONCEPTION, and pregnancy. Researchers also have come to recognize that hormones drive most primary cancers of the BREAST, uterus, PROSTATE GLAND, and testicles. New therapies use pharmaceutical interventions (synthetic hormones and chemicals that mimic the structure and action of hormones) to treat or prevent these cancers.

A

acromegaly A condition in which the PITUITARY GLAND secretes excessive GROWTH HORMONE (GH), causing the bones to thicken and become overgrown. This excessive growth is most apparent in the facial features and the extremities, especially the jaw, brow, hands, and feet. Most commonly acromegaly develops in midlife. When acromegaly occurs before the growth plates in the long bones of the arms and legs have fused, excessive height results. Doctors call this gigantism rather than acromegaly, though it is the same disease process. When excessive secretion of GH takes place after the growth plates have fused (generally after PUBERTY), the bones enlarge by thickening and spreading. This pattern of overgrowth results in the distortions characteristic of the disorder.

A BOND ACROSS TIME

Some medical historians believe the biblical giant Goliath and the sixteenth president of the United States, Abraham Lincoln (1809–1865), had in common the disorder of acromegaly. Both were exceedingly tall for the time in which they lived. Descriptions of Goliath and photographs of Lincoln suggest the characteristic features of acromegaly: overgrown facial features, excessive height, and unusually large hands and feet. Lincoln's headaches and fatigue, widely known, also were indications of acromegaly.

Though the small number of people doctors diagnose with acromegaly gives the perception this condition is rare, endocrinologists believe acromegaly is much more common than those numbers suggest. Acromegaly typically develops over years to decades, with symptoms emerging slowly and often nonspecifically. Many people learn they have acromegaly during evaluation for other conditions that could account for their symptoms, such as HYPERTENSION (high BLOOD PRESSURE) or DIABETES.

The most common cause of acromegaly is an ADENOMA (noncancerous tumor) in the anterior lobe of the pituitary gland, increasing the quantity of cells that secrete GH. Occasionally an adenoma or, rarely, an ADENOCARCINOMA (an adenoma that has turned cancerous) that secretes GH and is located elsewhere in the body, such as the gastrointestinal tract (notably the PANCREAS) or the LUNGS, is responsible. Growth hormone does not itself cause growth but instead stimulates the LIVER and other structures to produce other hormones, known collectively as insulinlike growth factors, or IGFs (sometimes called somatotropin mediators or somatomedins), that increase the rate at which cells divide. The most prominent of these is INSULIN growth factor 1 (IGF-1). High GH secretion results in excessive IGF-1 circulating in the BLOOD, which becomes one of the clinical markers for making the diagnosis.

Symptoms and Diagnostic Path

Often the earliest symptoms of acromegaly are gradual changes in the hands and feet, especially swelling of the palms and soles. A person may need larger sizes of shoes or gloves than usual and find that rings or watches no longer fit. Other symptoms include

- frequent headaches and vision disturbances
- excessive sweating and body odor
- thickened, often darkened, SKIN and NAILS
- increasing space between the TEETH
- PAIN in the joints

- DYSMENORRHEA (abnormal MENSTRUATION) in women and ERECTILE DYSFUNCTION in men
- weakness and fatigue

Headaches and visual disturbances occur when the pituitary adenoma grows large enough to create pressure against structures of the BRAIN. Often this pressure affects the OPTIC NERVE, which passes near the pituitary gland, causing an array of vision disturbances. The excessive GH causes the SWEAT GLANDS to enlarge and increase production, causing the unpleasant body odor and excessive sweating. The overgrowth of BONE in the jaws displaces the teeth, often first apparent as a shift in bite (the way the teeth meet when chewing).

There are no definitive tests to diagnose acromegaly, requiring the endocrinologist to compile a picture of clinical and observational findings. About a third of people who have acromegaly have elevated GH levels in the blood an hour after they drink an oral GLUCOSE solution. Because of the constant interactivity between GH, insulin, and glucose, GH stays in the blood circulation for only a short time, and its levels vary widely in a healthy person. The level of IGF-1 is more indicative of excessive GH secretion because IGF-1 stays in the circulation for an extended time. However, IGF-1 levels naturally diminish with age and in conditions such as OBESITY and diabetes.

Because endocrine functions are so tightly integrated, often the endocrinologist will measure the blood levels of other hormones, such as those the THYROID GLAND, ADRENAL GLANDS, and sex glands produce. Other diagnostic procedures may include imaging studies such as X-rays to identify changes in bone structure and MAGNETIC RESONANCE IMAGING (MRI) to determine whether a pituitary adenoma is present. The endocrinologist also may ask to see photographs of the person taken over the preceding 5 to 10 years to evaluate changes in physical structure and appearance.

Treatment Options and Outlook

The optimal treatment is an OPERATION to remove the pituitary adenoma. The surgeon reaches the tumor from an incision made inside the NOSE, entering the brain from the nasal cavity (called transsphenoidal resection). Therapies such as medications or radiation therapy may be necessary to shrink tumors larger than 10 centimeters (4 inches) or to treat tumors when surgery is not a viable option or cannot remove all of the tumor. In most people the surgery results in immediate relief of pressure-related symptoms such as HEADACHE and VISION IMPAIRMENT as well as a prompt return to normal levels of GH in the bloodstream. Many of the other symptoms then improve, though some of the changes the excessive GH has caused, such as bone overgrowth, remain.

MEDICATIONS TO TREAT ACROMEGALY

bromocriptine (Parlodel)
octreotide (Sandostatin)
pegvisomant (Somavert)

About a third of people who develop acromegaly also develop hypertension, resulting from the altered hormonal environment in the body, and HEART FAILURE, a consequence of the enlargement of the HEART in response to the excessive GH. Many also develop chronic OSTEOARTHRITIS, resulting from the overgrowth of CARTILAGE at the bone ends and the joints, and peripheral NEUROPATHY, resulting from overgrown tissues compressing the nerves. Often, these problems are what cause people to seek medical attention.

In health the interactions among GH, insulin, and SOMATOSTATIN regulate the hormonal balance that allows appropriate growth. In acromegaly, the excessive GH throws the equilibrium of this matrix out of kilter. As a result, people who have acromegaly are also likely to develop type 2 diabetes as a consequence of hormonal disturbances within the insulin–glucagon–somatostatin matrix. Diabetes and other consequential conditions may require ongoing therapy even after treatment for the acromegaly restores normal GH secretion. People who have acromegaly have an increased risk for developing COLORECTAL CANCER, which arises from adenomas of the intestinal wall (intestinal polyps).

Risk Factors and Preventive Measures

There are no known risk factors or preventive measures for acromegaly. Early diagnosis provides

the ideal opportunity to remove or suppress the responsible tumor.

See also ADENOMA-TO-CARCINOMA TRANSITION; HORMONE; HYPERHIDROSIS; INTESTINAL POLYP.

Addison's disease Damage to or progressive failure of the adrenal cortex of the ADRENAL GLANDS, resulting in insufficient production of the hormones CORTISOL and ALDOSTERONE. The most common cause of Addison's disease, also called primary ADRENAL INSUFFICIENCY, is autoimmune, in which the IMMUNE SYSTEM attacks the cells of the adrenal cortex. Doctors do not know what precipitates such an attack. Other causes include events that can damage or destroy adrenal tissue such as INFECTION that infiltrates the adrenal gland tissue (notably TUBERCULOSIS), blunt trauma or other injury to the abdomen, and tumors. Because the body cannot make up for the lost function of the adrenal glands, treatment requires lifelong HORMONE THERAPY to provide adequate levels of cortisol and usually aldosterone as well. With treatment most people who have Addison's disease are able to enjoy normal lifestyles and activities, though must remain vigilant for indications of Addisonian crisis.

Addisonian Crisis (Adrenal Crisis)

Addisonian crisis, also called adrenal crisis, occurs when physical stress such as injury, infection, or illness increases the body's demand for cortisol beyond the capacity of the adrenal glands to produce. The body exhibits signs of SHOCK and cardiovascular shock, including extreme HYPOTENSION (low BLOOD PRESSURE), DYSPNEA (shortness of breath or difficulty BREATHING), and erratic HEART RATE.

Addisonian crisis is a life-threatening event that requires immediate injection of hydrocortisone and emergency medical care.

Prompt and appropriate medical intervention (injected hydrocortisone and supportive measures to sustain cardiovascular function) can restore normal functions. However, Addisonian crisis can quickly turn fatal. People who have Addison's disease often carry emergency doses of injectable hydrocortisone, with instructions for dosage, and should wear identification of some sort (bracelet or necklace) that identifies them as having Addison's disease so medical aid response can act promptly with the correct measures.

Symptoms and Diagnostic Path

One of the earliest, though nonspecific, symptoms of Addison's disease is craving salt and salty foods, which occurs because the aldosterone deficit allows the KIDNEYS to release excessive amounts of sodium into the URINE. Other symptoms also tend to be nonspecific and include

- fatigue and tiredness
- postural hypotension (drop in blood pressure when rising from a sitting position)
- loss of APPETITE and weight loss
- MUSCLE weakness
- hyperpigmentation (darkening of the SKIN)
- irritability
- irregular MENSTRUATION (women)

The diagnostic path includes blood tests to measure the amounts of potassium, sodium, GLUCOSE, cortisol, and ADRENOCORTICOTROPIC HORMONE (ACTH). Other tests typically include a cortisol challenge—ACTH stimulation and CORTICOTROPIN-RELEASING HORMONE (CRH) stimulation tests—to assess the body's ability to produce cortisol and diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) to visualize the hypothalamus, pituitary gland, or adrenal glands.

DISTINGUISHING FEATURES OF ADDISON'S DISEASE AND ADRENAL INSUFFICIENCY

Addison's Disease	Adrenal Insufficiency
normal ADRENOCORTICOTROPIC HORMONE (ACTH)	low ACTH
areas of HYPERPIGMENTATION	normal SKIN color
elevated BLOOD potassium level (HYPERKALEMIA)	normal blood potassium level
low blood sodium level (HYPONATREMIA)	normal blood sodium level
low blood GLUCOSE level (HYPOGLYCEMIA)	normal blood glucose level
deficient ALDOSTERONE production	normal aldosterone production

It is essential for the endocrinologist to distinguish between Addison's disease, which is primary adrenal insufficiency (the dysfunction originates with the adrenal cortex) and secondary adrenal insufficiency (the dysfunction arises from inadequate ACTH, or less commonly from inadequate CRH). Diagnostic test results make this distinction clear.

Treatment Options and Outlook

Treatment consists of medications (HORMONE therapy) to supplement or replace the adrenal hormones. Endocrinologists commonly prescribe oral hydrocortisone to supplement cortisol and fludrocortisone to supplement aldosterone. Medication dosages may change over time, and lifelong treatment is necessary. Circumstances that stress the body require additional medication, preferably in advance of the stress, when possible, to avert an Addisonian crisis. These circumstances include PREGNANCY, labor and delivery, surgery, and serious illness or injury.

Risk Factors and Preventive Measures

People who have other AUTOIMMUNE DISORDERS such as HYPOTHYROIDISM or type 1 DIABETES have an increased likelihood of developing the autoimmune form of Addison's disease. About 70 percent of people who have Addison's disease have the autoimmune form. There are no known preventive measures for Addison's disease.

See also CHRONIC FATIGUE SYNDROME; POLYGLANDULAR DEFICIENCY SYNDROME; STRESS AND STRESS MANAGEMENT; STRESS RESPONSE HORMONAL CASCADE.

adenoma A noncancerous tumor arising from epithelial cells that typically forms within glandular tissues or structures. An adenoma contains the same cells as the gland from which it arises, causing it to secrete the same hormones. The result is an excess of the HORMONE within the BLOOD circulation, which disrupts the endocrine balance to cause an array of symptoms specific to the hormone and its influences. Adenoma is a common cause of many acquired endocrine disorders and is usually treatable with surgery, medication, or RADIATION THERAPY. Adenomas that do not cause symptoms (asymptomatic) are exceedingly common, and researchers estimate as many as 35 percent of people have them.

The diagnostic path includes blood tests to measure blood levels of the hormone and imaging procedures to identify the adenoma's location. Because of the risk for an adenoma to become cancerous, endocrinologists prefer to surgically remove adenomas that cause symptoms. The surgery can be straightforward or complex, depending on the adenoma's location. In some circumstances the surgeon may need to remove the entire affected gland to remove the tumor, or may be unable to remove all of the adenoma. Either circumstance may make it necessary for the person to take long-term HORMONE THERAPY (with removal of the entire gland) or to take medication to suppress the tumor's activity. Endocrinologists often prefer to take a course of watchful waiting with asymptomatic adenomas rather than initiating any treatment.

See also ADENOMA-TO-CARCINOMA TRANSITION; INTESTINAL POLYP.

adrenal glands A pair of endocrine glands, sometimes called suprarenal glands, located one above each kidney. The right adrenal gland is clearly triangular in shape, and the left adrenal gland has more of a crescent shape. Pumpkin colored, each adrenal gland is about three inches long and two inches deep, and rises above the kidney one-half inch (left adrenal gland) to three-quarters inch (right adrenal gland). These differences are due to the asymmetrical placement of the KIDNEYS, with the left kidney placed higher than the right in the abdomen.

The adrenal gland consists of two structurally distinct divisions: the outer cortex and the inner medulla. The adrenal cortex, a thick rindlike structure that makes up about 90 percent of the adrenal gland structure, encloses the adrenal medulla. The adrenal cortex produces the steroid hormones ALDOSTERONE and CORTISOL, as well as ESTROGENS, PROGESTERONE, and TESTOSTERONE. The fibrous, soft inner structure of the adrenal gland, the adrenal medulla, secretes the peptide hormones DOPAMINE, EPINEPHRINE, and NOREPINEPHRINE.

The most familiar function of the adrenal glands is their management of the body's physiologic responses to stress, commonly identified as the fight-or-flight reaction. In response to NERVE and hormonal signals from the HYPOTHALAMUS, the

adrenal glands can flood cortisol, epinephrine, and norepinephrine into the BLOOD circulation. On a mundane basis the adrenal glands also broadly regulate myriad functions of survival, such as BLOOD PRESSURE and HEART RATE, continuously adjusting the levels of these hormones in the bloodstream to meet the body's daily needs.

ADRENAL HORMONES

Adrenal cortex
ALDOSTERONE
CORTISOL
ESTROGENS
PROGESTERONE
TESTOSTERONE
Adrenal medulla
DOPAMINE
EPINEPHRINE
NOREPINEPHRINE

The Adrenal Cortex

The primary hormones of the adrenal cortex—aldosterone and cortisol—regulate many functions necessary for survival. Cortisol directs numerous chemical interactions that facilitate GLUCOSE balance and are integral for carbohydrate and fat METABOLISM. Aldosterone regulates the sodium–potassium balance, maintaining appropriate blood volume and blood pressure. The adrenal cortex arises from the same tissue in the EMBRYO as the sex glands (OVARIES and TESTES) and retains a functional connection to them in that it also synthesizes and secretes estrogen, progesterone, and testosterone in males and females alike. These hormones have numerous roles in functions other than those of reproduction. Testosterone helps maintain MUSCLE mass and BONE DENSITY; estrogen is essential for cholesterol metabolism; and the adrenal cortex needs progesterone to synthesize aldosterone.

The adrenal gland has three distinct layers, or zones, each of which exclusively produces specific hormones. These zones are

- The zona glomerulosa, the outermost zone, synthesizes and secretes aldosterone under the regulation of ADRENOCORTICOTROPIC HORMONE (ACTH) and the enzyme angiotensin II (synthesized when the kidneys release RENIN).
- The zona fasciculata, the middle zone, synthesizes and secretes cortisol under the regulation of ACTH.
- The zona reticularis, the innermost zone, synthesizes and secretes sex hormones (estrogen, progesterone, and testosterone) under the primary regulation of ACTH with secondary influence from FOLLICLE-STIMULATING HORMONE (FSH) and LEUTEINIZING HORMONE (LH).

The Adrenal Medulla

The adrenal medulla develops from the same tissue as the NERVOUS SYSTEM and remains under neurologic control. The adrenal medulla produces the hormones dopamine, epinephrine (also called adrenaline), and norepinephrine (also called noradrenaline). These function in the body as hormones, facilitating chemical interactions among cells, and as neurotransmitters, facilitating the passage of nerve signals. The interactions occur within the adrenal gland as well; the adrenal medulla needs cortisol to synthesize epinephrine.

BODY AND BRAIN: SAME CHEMICALS, DIFFERENT CONCENTRATIONS

The adrenal medullary hormones DOPAMINE, EPINEPHRINE, and NOREPINEPHRINE are the same chemical composition as their NEUROTRANSMITTER counterparts in the BRAIN. However, the brain requires much higher concentrations of these substances than the body can tolerate. A protective mechanism called the BLOOD–BRAIN BARRIER, a membranous layer of cells in the BLOOD vessels of the brain, regulates the size of molecules that can enter and leave the brain's circulation. The molecules of these hormones are too large to pass through, keeping the body (central) and brain supplies of them separate.

Kidney Disease and Adrenal Function

RENAL FAILURE, RENAL CANCER, and KIDNEY TRANSPLANTATION may affect various aspects of adrenal function. When the kidneys fail, they stop producing the hormone renin, which is essential for blood pressure regulation within the renin–angiotensin–aldosterone (RAA) system. The kidneys release renin when blood volume drops as a hormonal signal to the adrenal cortex to release

aldosterone. Some people experience disruptions of the RAA hormonal matrix after kidney transplantation because the transplanted kidney may be slow to become fully functional. When this occurs the person may need medications to help regulate blood pressure and sodium–potassium balance.

Though a separate structure, the adrenal gland is in direct contact with the surface of the kidney. One of the three arteries that delivers oxygenated blood to the adrenal gland branches from the renal ARTERY before the renal artery reaches the kidney. NEPHRECTOMY (surgical OPERATION to remove the kidney) can disturb this blood supply and damage the adrenal gland. The risk of this is highest with total nephrectomy, such as when removing a kidney that has completely failed or when radical nephrectomy (removal of the kidney, URETER, adrenal gland, and substantial surrounding tissue) is necessary to treat kidney cancer. Though most people can adapt to having only one adrenal gland just as they can adapt to having only a single kidney, the loss of both adrenal glands requires lifelong HORMONE THERAPY to replace adrenal hormones (primarily cortisol and aldosterone, the hormones of the adrenal cortex, as other structures in the body also synthesize the hormones the adrenal medulla produces).

Adrenal Gland Disorders

The most common disorder affecting the adrenal glands is ADENOMA, a noncancerous tumor that secretes excessive hormones of the division of the adrenal gland (cortex or medulla) from which it arises. Most commonly adrenal adenomas typically develop in the zona fasciculata of the adrenal cortex, causing excessive secretion of cortisol (CUSHING'S SYNDROME). Adenomas that develop in the zona glomerulosa cause excessive secretion of aldosterone (HYPERALDOSTERONISM). PHEOCHROMOCYTOMA, a tumor (usually noncancerous) that secretes epinephrine and norepinephrine, may form in the adrenal medulla.

CONDITIONS AFFECTING THE ADRENAL GLANDS

ADDISON'S DISEASE	adrenal ADENOMA
ADRENAL INSUFFICIENCY	CUSHING'S SYNDROME
HYPOALDOSTERONISM	PHEOCHROMOCYTOMA
POLYGLANDULAR DEFICIENCY SYNDROME	

For further discussion of the adrenal glands within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADENOMA-TO-CARCINOMA TRANSITION; AGING, ENDOCRINE CHANGES THAT OCCUR WITH.

adrenal insufficiency A condition, also called secondary adrenal insufficiency, in which the ADRENAL GLANDS fail to produce enough CORTISOL because there is not enough ADRENOCORTICOTROPIC HORMONE (ACTH) in the bloodstream. The cause may be damage to the PITUITARY GLAND that prevents it from synthesizing ACTH (such as a tumor), or extended therapy with CORTICOSTEROID MEDICATIONS (such as to treat some AUTOIMMUNE DISORDERS).

A tumor or its treatment may destroy the anterior lobe of the pituitary gland, preventing it from synthesizing ACTH. When this occurs permanent HORMONE THERAPY becomes necessary to maintain appropriate hormonal balance in the body, as the pituitary gland is the body's only source for ACTH.

During corticosteroid therapy, the high level of circulating corticosteroid in the bloodstream signals the HYPOTHALAMUS that no further release of cortisol is necessary. This inhibits the release of CORTICOTROPIN-RELEASING HORMONE (CRH), so there is no signal to the pituitary gland to release ACTH. In such circumstances adrenal insufficiency is more likely to happen when the person abruptly stops taking a corticosteroid medication rather than tapering it, though it can occur whenever a person takes corticosteroids for longer than four weeks. Though the body nearly always returns to normal HORMONE production in time, it is often necessary for the person to take supplemental hormone therapy in the interim.

Symptoms and Diagnostic Path

The symptoms of adrenal insufficiency are similar to those of ADDISON'S DISEASE and include

- tiredness and fatigue
- HYPOTENSION (low BLOOD PRESSURE)
- loss of APPETITE and weight loss
- MUSCLE weakness
- irritability

A history of recent (within several months) corticosteroid therapy is a strong indicator for adrenal insufficiency. The diagnostic path includes tests to measure the levels of potassium, sodium, GLUCOSE, cortisol, and ACTH in the blood. Other procedures typically include ACTH- and CRH-stimulation tests to assess the body's ability to produce cortisol. The endocrinologist may conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN to visualize and evaluate the pituitary gland and adrenal glands.

DISTINGUISHING FEATURES OF ADRENAL INSUFFICIENCY AND ADDISON'S DISEASE

Adrenal Insufficiency	Addison's Disease
low ACTH	normal ACTH
normal SKIN color	areas of hyperpigmentation
normal BLOOD potassium level	elevated blood potassium level (HYPERKALEMIA)
normal blood sodium level	low blood sodium level (HYPONATREMIA)
normal blood GLUCOSE level	low blood glucose level (HYPOGLYCEMIA)
normal ALDOSTERONE production	deficient aldosterone production

Treatment Options and Outlook

Treatment consists of medication (hormone therapy), typically oral hydrocortisone, to supplement adrenal production of cortisol until the pituitary gland returns to normal ACTH production. Most adrenal insufficiency resolves within a year of onset. When the cause of the adrenal insufficiency is permanent, such as damage to or destruction of the anterior lobe of the pituitary gland, permanent hormone therapy becomes necessary as well. During treatment it is important for the person to remain vigilant for signs of adrenal crisis, which requires emergency medical treatment. Circumstances that increase the risk for adrenal crisis include physiologic stress such as trauma, INFECTION, surgery, and PREGNANCY and CHILDBIRTH.

Risk Factors and Preventive Measures

The leading risk factor for adrenal insufficiency is corticosteroid therapy. The typical approach is to taper the corticosteroid DOSE gradually, to allow the body's normal hormonal mechanisms to resume. Abruptly stopping a corticosteroid medication after taking it for four weeks or longer greatly increases the risk for adrenal insufficiency.

See also CHRONIC FATIGUE SYNDROME; POLYGLANDULAR DEFICIENCY SYNDROME; STRESS AND STRESS MANAGEMENT.

adrenocorticotropic hormone (ACTH) A peptide HORMONE, also called corticotropin, the anterior lobe of the PITUITARY GLAND produces to stimulate the adrenal cortex of the ADRENAL GLANDS to synthesize and release CORTISOL. ACTH is one of the hormones in the STRESS RESPONSE HORMONAL CASCADE. The HYPOTHALAMUS releases the hormone CORTICOTROPIN-RELEASING HORMONE (CRH) to stimulate the pituitary's synthesis of ACTH. When cortisol levels reach the appropriate level in the bloodstream the hypothalamus shuts down its release of CRH and the pituitary gland subsequently ceases ACTH production until cortisol levels again drop. This cycle is ongoing as cortisol has numerous actions within the body, notably to facilitate carbohydrate and fat METABOLISM and suppress INFLAMMATION and other aspects of the IMMUNE RESPONSE.

For further discussion of ACTH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ALDOSTERONE; FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); PROLACTIN; THYROID-STIMULATING HORMONE (TSH).

aging, endocrine changes that occur with The endocrine system initiates many of the significant changes that mark the phases of life, from CONCEPTION to old age. Because critical endocrine processes slow with advancing age, many people believe the endocrine system holds the secrets to aging and thus the answers to slowing or preventing the changes that occur in the body that cause aging.

The most obvious endocrine changes that occur with age are those that regulate sexual maturation and reproduction. The onset of PUBERTY heralds the transition from childhood to adulthood and nearly every ENDOCRINE GLAND plays a role. The HYPOTHALAMUS steps up production and secretion of GONADOTROPIN-RELEASING HORMONE (GNRH), GROWTH

HORMONE–RELEASING HORMONE (GHRH), and THYROID-RELEASING HORMONE (TRH), initiating the hormonal cascades that generate tremendous growth spurts as well as the development of the secondary sex characteristics. The PITUITARY GLAND responds with accelerated secretion of FOLLICLE-STIMULATING HORMONE (FSH), GROWTH HORMONE (GH), LUTEINIZING HORMONE, AND THYROID-STIMULATING HORMONE (TSH) which in turn stimulate the gonads (OVARIES in females and TESTES in males) and affect METABOLISM in cells throughout the body. Surges in the sex hormones—ESTROGENS, PROGESTERONE, and TESTOSTERONE—complete the metamorphosis.

The hormonal changes that take place during PREGNANCY are among the most profound the human body experiences. The PLACENTA, the developing fetus's lifeline, produces dozens of hormones otherwise not found in the body. These hormones, coupled with hormonal changes in the woman's body, sustain the woman's body as a supportive environment for the unborn child and prepare it for further support (lactation) after birth. The hormones of pregnancy allow the muscles and ligaments of the abdomen to soften stretch to accommodate the enlarging UTERUS, increase the woman's BLOOD supply and metabolism (including thyroid hormones and INSULIN production), and increase vital functions such as BLOOD PRESSURE and HEART RATE.

Over the subsequent four or so decades the reproductive hormonal cascades slow. By midlife women end FERTILITY and enter MENOPAUSE, the cessation of MENSTRUATION and OVULATION. Rapid drops in estrogen and progesterone elicit major changes in a woman's body. The changes in men are less dramatic though nonetheless apparent. Testosterone levels peak around age 22 and steadily decline, tapering by age 60 to about 50 percent of peak levels. Men notice redistribution of body fat, decreased MUSCLE mass, and thinning scalp HAIR.

Also with advancing age levels of the hormones of the adrenal cortex, particularly cortisol, begin to decline. This affects body functions ranging from blood pressure and heart rate to immune response and GLUCOSE metabolism. These changes are among the changes some researchers believe hold the key to slowing, halting, or even reversing some of the events and consequences of aging. Accompanying these and other endocrine changes that occur with advancing age are increased risks for numerous health conditions such as CARDIOVASCULAR DISEASE (CVD), DIABETES, LIVER disease, and kidney disease. Nearly all hormonal production and endocrine processes diminish by age 80, and the body itself slows.

See also ANTI-AGING APPROACHES; LIFE EXPECTANCY; LIFESTYLE AND HEALTH.

aldosterone A steroid HORMONE the adrenal cortex of the ADRENAL GLANDS produces that plays a key role in regulating BLOOD PRESSURE. Aldosterone is vital for life; the body can sustain its functions for only a few days without it. Chemically aldosterone is a mineralocorticosteroid, a type of steroid (cholesterol-based structure) that influences the body's balance of minerals such as sodium and potassium. Aldosterone targets cells in the KIDNEYS that regulate the amounts of these minerals which remain in the bloodstream. The adrenal cortex releases aldosterone when the amount of potassium in the BLOOD increases or when the kidneys release the hormone RENIN in response to decreased blood volume flowing through the kidneys. Renin initiates a series of enzyme conversions that result in the production of angiotensin II, which then stimulates aldosterone production in the adrenal cortex.

LICORICE AND ALDOSTERONE

Long-term, excessive consumption of natural licorice (*Glycyrrhiza glabra* extract or glycyrrhizic acid) interferes with aldosterone binding and allows aldosterone levels in the BLOOD to rise, establishing symptoms similar to those HYPERALDOSTERONISM. Doctors call the resulting condition pseudo-hyperaldosteronism. Most licorice-flavored candies and other products in the United States do not contain natural licorice. However, natural licorice is an ingredient in many products in other countries, notably in Europe.

The release of aldosterone increases sodium retention in the blood and potassium excretion into the URINE, raising levels of sodium and dropping the levels of potassium in the blood. The higher sodium level correspondingly draws more water into the blood, increasing the blood volume.

Aldosterone also acts on the peripheral arterioles, the tiny arteries within the tissues, causing them to constrict. The combined effect of increased blood volume and peripheral vasoconstriction causes blood pressure to rise. This is a fundamental cascade of one of the body's primary blood pressure–regulatory mechanisms, the renin–angiotensin–aldosterone (RAA) system. Some medications to treat congestive HEART FAILURE and HYPERTENSION (high blood pressure) work by blocking the action of aldosterone.

Aldosterone deficiency, such as may result with ADRENAL INSUFFICIENCY and ADDISON'S DISEASE, causes HYPOTENSION (low blood pressure) and electrolyte imbalances that can cause ARRHYTHMIA (disturbance of the HEART's rhythm and rate). Untreated aldosterone deficiency is fatal. Treatment with hormone-replacement therapy restores homeostasis. Excessive aldosterone in the bloodstream (HYPERALDOSTERONISM) typically results from an adrenal ADENOMA (noncancerous tumor) arising from the middle section of the adrenal cortex, the zona fasciculata, which produces aldosterone.

For further discussion of aldosterone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIC HORMONE (ACTH); CORTICOTROPIN-RELEASING HORMONE (CRH); CORTISOL; DOPAMINE; EPINEPHRINE; NOREPINEPHRINE.

amyloidosis An uncommon and potentially fatal disorder of METABOLISM in which the BONE MARROW produces defective antibodies that result in an abnormal protein, amyloid. The amyloid leaves the bone marrow in the BLOOD and forms fibrous deposits in organs and tissues throughout the body. The deposits interfere with normal functions, which can result in severe damage to and failure of organs such as the HEART, LIVER, and KIDNEYS. Amyloid deposits can also accumulate in the nerves and NERVOUS SYSTEM, LYMPH NODES, and blood vessels. There are three forms of amyloidosis: primary, secondary, and hereditary.

Primary amyloidosis Primary amyloidosis, also called idiopathic amyloidosis, occurs independently of other disease processes and without known cause (idiopathic). Most people who have amyloidosis have this form, which tends to affect the heart, LUNGS, THYROID GLAND, liver, intestines, SKIN, and tongue.

Secondary amyloidosis Secondary amyloidosis accompanies or occurs as a consequence of other disease processes. The most common association is with MULTIPLE MYELOMA, a CANCER of the lymph system. About 15 percent of people who have multiple myeloma develop secondary amyloidosis. Secondary amyloidosis also may occur in conjunction with chronic inflammatory disorders such as RHEUMATOID ARTHRITIS or with chronic INFECTION such as TUBERCULOSIS and OSTEOMYELITIS. Secondary amyloidosis tends to affect the liver, SPLEEN, kidneys, ADRENAL GLANDS, and lymph nodes.

Hereditary amyloidosis Rarely, a person inherits amyloidosis as a result of genetic MUTATION. The amyloid deposits in hereditary amyloidosis are most likely to accumulate in the heart, kidneys, intestines, vitreous humor (the gelatinous substance inside the EYE), and PERIPHERAL NERVES.

Symptoms and Diagnostic Path

Symptoms of amyloidosis vary, depending on the organ systems affected. Many people experience generalized symptoms such as weakness, tiredness and fatigue, and unexplained weight loss. Other symptoms that may occur with amyloid deposits in specific organs or systems include

- DIARRHEA (gastrointestinal)
- tingling and numbness in the hands and feet (nerves)
- ARRHYTHMIA (irregularities in the heartbeat; heart)
- swollen tongue and difficulty swallowing (tongue; gastrointestinal; nerves)
- DYSPNEA (shortness of breath; lungs, heart)
- HEPATOMEGALY (enlarged liver; liver)

Amyloidosis also may manifest through symptoms of disease process such as HYPOTHYROIDISM (amyloid deposits in the thyroid gland) and kidney failure (amyloid deposits in the kidneys). The diagnostic path includes clinical assessment of symptoms, blood and URINE tests that may detect

the presence of abnormal proteins, and biopsy of representative amyloid deposits.

Treatment Options and Outlook

There is no curative treatment for amyloidosis. When amyloidosis is secondary, treatment for the underlying condition often mitigates the symptoms and progression of the amyloidosis. Treatment for primary amyloidosis targets symptom relief. In some people, a regimen of CHEMOTHERAPY halts the amyloidosis progression for up to several years. Kidney, heart, or liver transplantations are sometimes viable options when amyloid deposits accumulate in these organs. STEM CELL transplantation shows promise for long-term relief, though existing amyloid deposits remain in the tissues. Many people are able to control their symptoms for long periods of time through carefully selected therapeutic measures.

Risk Factors and Preventive Measures

There are no known risk factors or preventive measures for primary amyloidosis. Multiple myeloma and chronic inflammatory disorders and infections are significant risk factors for secondary amyloidosis. Amyloidosis is more likely to develop when these conditions are long-term and poorly controlled. Though it is not possible to prevent secondary amyloidosis, prompt and appropriate treatment for the underlying condition may mitigate its manifestation.

See also CHRONIC FATIGUE SYNDROME; FAMILIAL MEDITERRANEAN FEVER; INFLAMMATION; ORGAN TRANSPLANTATION; SARCOIDOSIS.

androgens A collective term for the "male" sex hormones, prohormones (chemical precursors the body converts to hormones), and metabolites (byproducts of HORMONE METABOLISM). Androgens are steroid hormones the body synthesizes from cholesterol; they are variably anabolic (they build MUSCLE mass, some more actively than others). Androgens are also the precursors (starting point) for the ESTROGENS ("female" sex hormones). The most abundant and familiar androgen is TESTOSTERONE. In addition to establishing male secondary sex characteristics and FERTILITY, androgens have multiple functions in men and women both with regard to muscle mass and STRENGTH, BONE DENSITY, LIBIDO (sex drive), and metabolism.

Men and women alike have androgens (just as both sexes also have estrogens). The gonads, or sex glands (OVARIES in women and TESTES in men), synthesize (produce) most of the androgens in the BLOOD circulation. The adrenal cortex of the ADRENAL GLANDS and adipose (fat) cells also synthesize androgens. The HYPOTHALAMUS's secretion of GONADOTROPIN-RELEASING HORMONE (GNRH) regulates the hormonal cascade for endogenous (within the body) androgen production and release. Some androgens are available as exogenous supplements used to treat disorders of androgen deficiency as well as taken illicitly to enhance athletic performance.

ENDOGENOUS ANDROGENS

androstane	androstanediol
androstenedione	androstenolone
androsterone	DEHYDROEPIANDROSTERONE (DHEA)
dihydrotestosterone	TESTOSTERONE

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; HIRSUTISM; HORMONE THERAPY; HYPOGONADISM; INFERTILITY; INSULIN RESISTANCE; POLYGLANDULAR DEFICIENCY SYNDROME; PROSTATE CANCER; SPERMATOGENESIS.

antidiuretic hormone (ADH) A peptide HORMONE, also called vasopressin, the HYPOTHALAMUS synthesizes (produces) and the posterior lobe of the PITUITARY GLAND stores and releases. ADH regulates the amount of water the KIDNEYS withhold in the bloodstream. The hypothalamus signals the pituitary gland to release ADH when the body needs additional fluid, such as during excessive sweating with heat or intense exercise. Increased ADH in the BLOOD causes the kidneys to withhold more water from the circulating blood, raising blood volume and decreasing URINE production. In high concentrations, ADH acts to constrict peripheral arterioles (the smallest arteries deep in the tissues). In combination, these effects are among the body's mechanisms for regulating BLOOD PRESSURE. Dysfunction of the pituitary gland, and less commonly the hypothalamus, can result in inadequate levels of ADH in the bloodstream, causing the rare

condition DIABETES INSIPIDUS (which is not the same disease process as DIABETES mellitus, a disorder of INSULIN production or METABOLISM). Kidney disease may also interfere with the ability of the kidneys to respond to ADH.

For further discussion of ADH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ALDOSTERONE; FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); OXYTOCIN; PROLACTIN; RENIN; THYROID-STIMULATING HORMONE (TSH).

C

calcitonin A peptide HORMONE the THYROID GLAND produces that increases the amount of calcium the bones can accept. Calcitonin functions in synchronization with PARATHYROID HORMONE, which the PARATHYROID GLANDS secrete, to maintain calcium balance in the BLOOD and in the body. Calcium is essential for BONE DENSITY and STRENGTH, as well as for the conduction of NERVE impulses in MUSCLE tissue, including that of the HEART. The balance between calcitonin and parathyroid hormone maintains a constant level of calcium in the blood to allow proper nerve conduction for heart function as well as skeletal muscle function. This balance may come at the expense of the amount of calcium in the bones, however, which the body uses as a "bank" for the storage and withdrawal of calcium. Calcitonin facilitates calcium "deposit" to the bones by channeling calcium from the blood into the bones. It binds with receptor sites on the surfaces of osteoblasts, the cells within the bones that produce new BONE tissue.

A form of THYROID CANCER, medullary thyroid cancer, forms in the parafollicular cells that produce calcitonin. Excessive levels of calcitonin in the blood may indicate such a cancer. Disorders of the parathyroid glands that affect the secretion of parathyroid hormone may also disrupt the levels of calcitonin in the blood.

For further discussion of calcitonin within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also OSTEOPOROSIS; THYROXINE (T_4); TRIIODOTHYRONINE (T_3).

cholecystokinin See DIGESTIVE HORMONES.

chorionic gonadotropin A peptide HORMONE of PREGNANCY that the fertilized ovum (egg) secretes to stimulate the corpus luteum to continue producing PROGESTERONE, which maintains an environment within the UTERUS to support the implantation of the EMBRYO. The corpus luteum, a temporary endocrine structure, develops in an ovarian follicle after the follicle releases an ovum, marking the start of OVULATION. The corpus luteum then begins secreting progesterone, which causes the lining of the uterus to thicken and its BLOOD supply to enrich in preparation for pregnancy. Without chorionic gonadotropin the corpus luteum deteriorates and the uterine lining sloughs away (MENSTRUATION). About eight weeks into pregnancy the PLACENTA forms and takes over chorionic gonadotropin production, which continues until birth. Pregnancy tests measure the amount of chorionic gonadotropin in the URINE or the blood. Fertility specialists use injections of chorionic gonadotropin (called human chorionic gonadotropin, or hCG, in its pharmaceutical form) to stimulate ovulation in women and TESTOSTERONE production, to encourage SPERM production, in men.

For further discussion of chorionic gonadotropin within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; CONCEPTION; ESTROGENS; FERTILITY; OXYTOCIN; PROLACTIN; RELAXIN.

corticotropin-releasing hormone (CRH) A peptide HORMONE the HYPOTHALAMUS synthesizes and releases in response to endocrine and neurologic signals that report the status of the body's vital functions. CRH is one of the hormones in the

STRESS RESPONSE HORMONAL CASCADE and stimulates the anterior lobe of the PITUITARY GLAND to produce ADRENOCORTICOTROPIC HORMONE (ACTH). ACTH in turn stimulates the ADRENAL GLANDS to release CORTISOL, a steroid hormone that has numerous actions in the body. The level of cortisol in the bloodstream is one of the endocrine signals that determines the release of CRH. The hypothalamus also releases CRH in a rhythmic pattern that coincides with the body's circadian cycle of sleep and wake. CRH levels peak just before dawn and trough just before dusk, establishing higher ACTH and cortisol levels during the waking hours.

For further discussion of CRH within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also GONADOTROPIN-RELEASING HORMONE (GNRH); GROWTH HORMONE–RELEASING HORMONE (GHRH); THYROTROPIN-RELEASING HORMONE (TRH).

cortisol A HORMONE the adrenal cortex of the ADRENAL GLANDS produces. Chemically cortisol is a glucocorticosteroid, a type of steroid (cholesterol-based structure) that influences carbohydrate and fat METABOLISM (GLUCOSE balance) in the body. Cortisol is the main player in the STRESS RESPONSE HORMONAL CASCADE, essential for activating other hormones and chemical processes required for many vital functions within the body. All cells in the body have receptors for cortisol. The body requires a minimum level of cortisol in the bloodstream, as well as increased amounts of cortisol to respond to stress by raising BLOOD PRESSURE, HEART RATE, BREATHING, and metabolic rate. Cortisol also counters the body's IMMUNE RESPONSE, helping to subdue areas of INFLAMMATION after they develop.

Cortisol levels fluctuate in a rhythmic pattern over the course of 24 hours, being highest during waking hours when the body is most active and lowest a few hours after falling asleep. To maintain this pattern the HYPOTHALAMUS initiates a cascade of hormonal activity by releasing CORTICOTROPIN-RELEASING HORMONE (CRH) in synchronization with the body's circadian rhythm (cycle of wake and sleep). CRH stimulates the anterior lobe of the PITUITARY GLAND to release ADRENOCORTICOTROPIN HORMONE (ACTH). ACTH in turn causes the adrenal cortex to produce and release cortisol. When the BLOOD level of cortisol is adequate, the hypothalamus ceases release of CRH, the pituitary gland ends release of ACTH, and the adrenal cortex stops cortisol production. When the cortisol level in the blood drops or physiologic sensors (such as barosensors that detect changes in blood pressure) indicate a need to respond to stress the hypothalamus again boosts CRH output.

Cortisol production increases in response to physiologic stress such as intense physical exercise, as well as to emotional stress such as fear or anger. Research suggests that persistently elevated cortisol levels result in long-term damage to the cardiovascular system, notably contributing to HYPERTENSION (high blood pressure) and ARTERIOSCLEROSIS (stiffening of the arteries). Chronically insufficient levels of cortisol in the blood result in ADDISON'S DISEASE; chronically excessive levels of cortisol in the blood result in Cushing's syndrome. People who take long-term CORTICOSTEROID MEDICATIONS to treat chronic inflammatory conditions may develop acquired Cushing's syndrome, also called hyperadrenocorticism. Pharmaceutical preparations of cortisol commonly used as anti-inflammatory medications are cortisone and hydrocortisone.

For further discussion of cortisol within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ALDOSTERONE; DOPAMINE; EPINEPHRINE; NOREPINEPHRINE; STRESS AND STRESS MANAGEMENT; WORKPLACE STRESS.

Cushing's syndrome A constellation of symptoms that occur as a consequence of high levels of CORTISOL in the bloodstream. Cushing's syndrome may result from long-term CORTICOSTEROID MEDICATIONS (exogenous Cushing's syndrome) or from excessive cortisol production within the body (endogenous Cushing's syndrome). Untreated Cushing's syndrome affects many vital functions including BLOOD PRESSURE and HEART RATE, and can be fatal.

Exogenous Cushing's Syndrome

Exogenous Cushing's syndrome is the more common form of this condition and typically occurs in

people taking long-term corticosteroid therapy to suppress the IMMUNE RESPONSE such as following ORGAN TRANSPLANTATION (to prevent GRAFT VS. HOST DISEASE and organ rejection) or to treat chronic inflammatory conditions such as ASTHMA, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), RHEUMATOID ARTHRITIS, SARCOIDOSIS, and INFLAMMATORY BOWEL DISEASE (IBD). Occasionally multiple corticosteroid injections into inflamed joints can also produce exogenous Cushing's syndrome.

Endogenous Cushing's Syndrome

Cushing's disease is an older term for endogenous Cushing's syndrome, which most commonly occurs as a result of adrenal or pituitary ADENOMA (noncancerous tumor) that increases cortisol secretion. A pituitary adenoma causes the anterior lobe of the PITUITARY GLAND to produce excessive ADRENOCORTICOTROPIC HORMONE (ACTH). The ACTH stimulates the adrenal cortex of the ADRENAL GLANDS to secrete cortisol. An adrenal adenoma develops in the adrenal cortex and itself secretes cortisol independent of ACTH stimulation.

Other causes of endogenous Cushing's syndrome include adrenal hypertrophy (enlargement of the adrenal glands), which increases cortisol secretion, and ACTH-secreting tumors located elsewhere in the body such as some cancers of the lung, PANCREAS, and BREAST. As with pituitary adenoma, the ACTH secretion stimulates the adrenal cortex to increase cortisol production. Cushing's syndrome is sometimes one of the earliest indications of small-cell LUNG CANCER (SCLC), the tumors of which are characteristically ACTH secreting.

Symptoms and Diagnostic Path

The symptoms and signs of Cushing's syndrome are the same regardless of the condition's cause and typically include

- a rounded, flushed face ("moon face")
- transition to an "apple" body shape: thickened trunk due to accumulated abdominal fat and thinned arms and legs due to MUSCLE atrophy (wasting)
- accumulation of fat in a "hump" between the shoulder blades
- HIRSUTISM (increased body HAIR) and ACNE
- HYPERTENSION (high blood pressure)
- delayed wound HEALING and decreased resistance to INFECTION
- irritability, DEPRESSION, mood swings, and difficulty concentrating

The diagnostic path begins with BLOOD and URINE tests to measure the body's levels and excretion of cortisol. When the endocrinologist suspects exogenous Cushing's syndrome due to corticosteroid therapy, these tests are often conclusive for the diagnosis. The endocrinologist may conduct additional tests to assess the body's response to dexamethasone (a corticosteroid) and ACTH (dexamethasone test and ACTH-stimulation test, respectively) when endogenous Cushing's syndrome is likely. Imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) can reveal structural abnormalities, including tumors, of the pituitary gland and the adrenal glands.

Treatment Options and Outlook

Treatment targets reducing the amount of cortisol in the blood circulation. With exogenous Cushing's syndrome, treatment usually means transitioning to noncorticosteroid medications to manage the underlying condition and its symptoms. Treatment in endogenous Cushing's syndrome may be surgery to remove or RADIATION THERAPY to shrink a pituitary or adrenal adenoma, appropriate treatment for an ACTH-secreting tumor located elsewhere in the body, or medications such as ketoconazole or mitotane to suppress ACTH or cortisol synthesis. Some people require HORMONE THERAPY (sometimes long-term) to supplement or replace adrenal or pituitary hormones after treatments that target the gland directly.

Risk Factors and Preventive Measures

The primary risk factor for exogenous Cushing's syndrome is corticosteroid therapy. Transitioning to noncorticosteroid medications generally relieves Cushing's syndrome symptoms and often prevents the condition from developing. However, noncorticosteroid medications may have undesired side effects or be less effective in controlling the underlying condition for which the doctor prescribes

them. Endogenous Cushing's syndrome is not preventable though early diagnosis minimizes its consequences and affords a wider range of treatment.

See also ADDISON'S DISEASE; ADRENAL INSUFFICIENCY; POLYCYSTIC OVARY SYNDROME (PCOS); POLYGLANDULAR DEFICIENCY SYNDROME.

D

dehydroepiandrosterone (DHEA) A precursor steroid HORMONE the adrenal cortex of the ADRENAL GLANDS synthesizes from cholesterol. The OVARIES or TESTES, and to a lesser extent the adrenal cortex, further formulate DHEA into TESTOSTERONE and ESTROGENS. LUTEINIZING HORMONE (LH) provides the hormonal stimulus for this synthesis. Levels of DHEA in the BLOOD circulation begin to rise around age 10, preceding the onset of PUBERTY, and peak in the mid-20s. DHEA levels in the bloodstream decline by about 15 percent a decade until about age 75, at which point the level stabilizes at about 15 percent of what it was at its peak 50 years earlier. Though there is speculation that diminishing DHEA levels may in some way precipitate the changes that take place with aging, researchers have yet to identify the mechanisms responsible.

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; DHEA SUPPLEMENT.

diabetes A condition, clinically known as diabetes mellitus, in which the ISLETS OF LANGERHANS do not produce enough INSULIN or the body's cells do not appropriately respond to insulin, resulting in an inability of the cells to accept GLUCOSE. There are three major forms of diabetes: type 1, type 2, and gestational. Lifestyle factors significantly influence the development and course of diabetes, particularly type 2. Diabetes is the most common endocrine disorder.

Diabetes is a significant health concern in the United States, with more than 13 million people knowing they have the condition. Another 5 or 6 million have diabetes though are unaware. Diabetes is the sixth leading cause of death in the United States, directly claiming 70,000 lives each year. As a leading cause of CARDIOVASCULAR DISEASE (CVD), kidney disease, and RENAL FAILURE, diabetes contributes to thousands more deaths as well. Diabetes is also the primary cause of VISION IMPAIRMENT and blindness, and a significant cause of peripheral NEUROPATHY (NERVE damage), among American adults.

Medical texts that are several thousand years old make reference to diabetes. Ancient physicians identified diabetes as the "honey URINE" disease, a moniker that became refined through the centuries to the somewhat less graphic "sugar diabetes." Until the discovery of insulin in the early 1920s, the diagnosis of diabetes was a death sentence. Efforts to manage the disease by restricting sugar were futile because the true problem was not too much sugar but rather not enough insulin.

As researchers and doctors gained greater understanding of diabetes, they realized it was insulin that made possible glucose's entry into the cells. Doctors now know diabetes results from the body's inability to produce or use insulin, which allows glucose (sugar) to accumulate in the BLOOD and spill over into the urine. Insulin therapy became the breakthrough in treatment that restored the potential for relatively normal lives for those who developed diabetes.

Type 1 Diabetes

Type 1 diabetes is an autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack and destroy the cells of the islets of Langerhans. As a result, the body cannot produce insulin. An interplay between genetic and environmental factors is likely, with some researchers suspecting the autoimmune reaction follows INFECTION with a VIRUS. People who have type 1 diabetes must take regular insulin injections to meet their insulin needs and check their blood glucose levels

frequently to maintain as tight of a balance as possible between insulin and glucose. Type 1 diabetes most often develops before the age of 20, giving rise to its former designation as juvenile diabetes. Onset is usually rapid and pronounced. Type 1 diabetes requires lifelong insulin therapy.

Before current treatments many people who developed type 1 diabetes died from the condition or its complications before living much longer than early adulthood, making this a disease of the young. However, treatment approaches are significantly improved and many people who have type 1 diabetes now live well into old age with careful medical and lifestyle management. Some people refer to type 1 diabetes as insulin-dependent diabetes, which is no more accurate than the term juvenile diabetes because about 40 percent of people who have type 2 diabetes also require insulin therapy.

People who have type 1 diabetes have a higher likelihood of developing other AUTOIMMUNE DISORDERS of the endocrine system, notably thyroid conditions such as autoimmune THYROIDITIS and HYPOTHYROIDISM as well as autoimmune ADRENAL INSUFFICIENCY. Type 1 diabetes is also a component of complex endocrine disorders such as POLYGLANDULAR DEFICIENCY SYNDROME and MULTIPLE ENDOCRINE NEOPLASIA (MEN). Women who have well-controlled type 1 diabetes generally can conceive, carry, and deliver a PREGNANCY with few complications, though require close medical monitoring and diligent prenatal care. However, type 1 diabetes can affect FERTILITY in both women and men.

Type 2 Diabetes

Type 2 diabetes develops slowly, evolving over years and sometimes decades as a consequence of progressive INSULIN RESISTANCE. This form of diabetes most commonly develops in people who are age 50 or older, though can occur at any age (including childhood). A strong correlation exists between OBESITY and type 2 diabetes. Many health experts believe type 2 diabetes is fully preventable through lifestyle measures that incorporate nutritious EATING HABITS, daily physical exercise, and maintaining a healthy body weight. About 30 percent of people diagnosed with type 2 diabetes can control the condition through weight loss and lifestyle measures. The rest require oral antidiabetes medications or insulin therapy. Type 2 diabetes may occur as a component of complex endocrine disorders, notably insulin resistance, as well as secondary to endocrine disorders affecting the adrenal cortex such as CUSHING'S SYNDROME (the adrenal steroid CORTISOL influences glucose METABOLISM).

Gestational Diabetes

Gestational diabetes develops during pregnancy as a consequence of the demands pregnancy places on the mother's body. A pregnant woman requires up to three times as much insulin to meet the needs of her body and the growing FETUS. However, the hormones that support pregnancy increase insulin resistance, reducing the woman's ability to use the insulin her body produces. The consequence may be temporary type 2 diabetes. Gestational diabetes affects about 4 percent of pregnant women in the United States. Some women can maintain appropriate insulin and glucose levels through careful nutritional habits, daily exercise, and WEIGHT LOSS AND WEIGHT MANAGEMENT. Others may require insulin therapy (many oral antidiabetes medications are not approved for use during pregnancy) for the duration of pregnancy.

Untreated gestational diabetes can have serious consequences for the baby, as the high levels of insulin in the mother's blood circulation increase the amount of glucose the baby's body can accept. One consequence is an unusually large baby. Rapid fetal growth is one indication that a woman might have gestational diabetes. About 70 percent of women who develop gestational diabetes recover completely. The rest develop permanent type 2 diabetes, either continuing after the end of the pregnancy or years to decades later.

Symptoms and Diagnostic Path

The symptoms of diabetes are similar across the types, though in type 1 may be rapid and severe. These symptoms include

- excessive thirst and frequent urination
- unexplained weight loss
- increased APPETITE
- changes in vision
- tingling in the hands and feet

- tiredness and weakness
- wounds or sores that heal slowly, or frequent infections (notably CANDIDIASIS)

The diagnostic path begins with a fasting blood glucose test, which measures the amount of glucose in the blood circulation after 12 hours without food or beverages other than water. Two separate results with blood glucose levels of 126 milligrams per deciliter of blood (126 mg/dL) confirm the diagnosis. Another blood test is glycosylated hemoglobin (HbA_{1c}), which measures a protein that indicates the stability of blood glucose levels over time. Normal HbA_{1c} is 4 to 6 percent; HbA_{1c} greater than 8 percent supports the diagnosis of diabetes. The doctor may choose to conduct a glucose-tolerance test, which measures the body's ability to respond to a rapid influx of glucose.

Treatment Options and Outlook

Treatment depends on the form of diabetes. Type 1 diabetes requires lifelong insulin therapy. About a third of people who have type 2 diabetes can manage the condition through weight loss and lifestyle measures (nutritious eating habits, daily exercise, and weight management), while the remainder require oral antidiabetes medications or insulin therapy. Ultimately about 40 percent of people who have type 2 diabetes will require insulin therapy, however, the underlying insulin resistance tends to be progressive within the disease process as well as with advancing age. Women who have gestational diabetes may be able to control the condition through lifestyle measures or may require treatment with oral antidiabetes medications approved for use in pregnancy or insulin therapy for the duration of the pregnancy.

Insulin therapy Therapeutic insulin is an injectable solution self-administered through subcutaneous injection (shots) one to several times a day. Until the 1990s most insulin products were the purified extracts culled from porcine (pig) and bovine (cow) pancreases. The biochemical structures of these extracts were close enough to human insulin to work in the human body, though in some people the differences were significant enough to activate an IMMUNE RESPONSE. In the 1990s laboratories began using RECOMBINANT DNA technologies to create synthetic insulin products biochemically and immunologically identical to endogenous human insulin. These insulins now allow precise dosaging and predictable actions within the body. Insulin doses are uniquely individual and may also vary with the person's activity level and other health conditions such as infections that cause FEVER. People taking insulin therapy check their blood glucose levels on a regular basis (one to several times daily) using a glucometer, which requires a fingerprick sample of blood.

Oral antidiabetes medications In 1958 the first oral medication to treat type 2 diabetes, the new

INSULIN PRODUCTS

Type of Action	Insulin Products	Onset	Peak Activity	Duration
rapid	lispro (Humalog)	5 to 15 minutes	45 to 90 minutes	3 to 4 hours
	aspart (NovoLog)	10 to 20 minutes	1 to 3 hours	3 to 5 hours
short	regular (R)	30 minutes	2 to 5 hours	5 to 8 hours
intermediate	neutral protamine	1 to 3 hours	6 to 12 hours	16 to 24 hours
	hagedorn (NPH) + lente (L)	30 minutes	7 to 12 hours	16 to 24 hours
	premixed (R + NPH)			
long	ultralente	4 to 6 hours	8 to 20 hours	24 to 28 hours
very long	glargine (Lantus)	1 hour	evenly over 24 hours	24 hours

sulfonylurea DRUG chlorpropamide (Diabinese), received approval for use in the United States. Sulfonylurea stimulates the beta islet cells to increase insulin production, raising the level of circulating insulin the blood. Subsequent generations of sulfonylureas have become more potent, more predictable, and less likely to cause side effects and are the foundation for oral therapy for type 2 diabetes. New sulfonylureas as well as new kinds of drugs to improve insulin sensitivity and influence glucose metabolism became available in the 1980s and 1990s. Many people who require treatment beyond lifestyle measures for type 2 diabetes take combinations of antidiabetes medications for optimal individualized control.

ORAL ANTIDIABETES MEDICATIONS

Sulfonylureas	
acetohexamide (Dymelor)	chlorpropamide (Diabinese)
glimepiride (Amaryl)	glipizide (Glucotrol, Glucotrol Xl)
glyburide (DiaBeta)	glyburide (Glynase PresTab, Micronase)
tolazamide (Tolinase)	
tolbutamide (Orinase)	
Biguanides	
metformin (Glucophage, Glucophage XR)	
Alpha-glucosidase inhibitors	
miglitol (Glyset)acarbose (Precose)	
Thiazolidinediones	
pioglitazone (Actos)rosiglitazone (Avandia)	
Meglitinides	
repaglinide (Prandin)	
d-Phenylalanine derivatives	
nateglinide (Starlix)	
Combination products	
glyburide + metformin (Glucovance)	

Lifestyle measures Nutritious eating habits, daily physical exercise, and healthy weight are critical factors especially in type 2 diabetes. Physical exercise improves the sensitivity of cells to insulin, allowing the body to become more efficient with insulin production. Most people who have diabetes do not require special diets though must monitor their consumption of food types to remain in balance with their medications (oral or insulin). Health-care providers recommend that all people diagnosed with diabetes and their family members attend diabetes education workshops and classes available through hospitals and health-care clinics.

Risk Factors and Preventive Measures

Type 1 diabetes is not preventable, and likely results from an interaction of genetic and environmental factors that remain for researchers to identify. Type 2 diabetes, however, may be fully preventable through lifestyle choices that support healthy weight, nutritious eating habits, and daily physical activity. Long-term elevation of glucose in the blood causes extensive damage to the blood vessels and nerves. Complications of diabetes can be significant, though careful management of the diabetes can mitigate most of them. People who have any form of diabetes have increased risk for:

- CORONARY ARTERY DISEASE (CAD)
- HYPERTENSION (high BLOOD PRESSURE)
- RETINOPATHY of diabetes (damage to the RETINA)
- peripheral neuropathy (damage to the nerves)
- delayed wound HEALING and frequent infections, particularly a risk with the feet
- kidney disease and renal failure
- ERECTILE DYSFUNCTION in men and INFERTILITY in men and women

Most people who have diabetes are able to enjoy regular activities with appropriate treatment and lifestyle management.

See also ANTIBODY; DIABETES AND CARDIOVASCULAR DISEASE; DIABETES PREVENTION; HEALTH RISK FACTORS.

diabetes insipidus A condition of inadequate ANTIDIURETIC HORMONE (ADH) production or response. In health the HYPOTHALAMUS produces and the posterior lobe of the PITUITARY GLAND stores ADH. ADH acts on the KIDNEYS to regulate the amount of water they excrete into the URINE. The pituitary gland releases ADH when fluid levels in the body drop, causing the kidneys to withhold more water in the BLOOD. Diabetes insipidus can result from dysfunction of either the hypothalamus or the pituitary gland or disruption of communication between the two endocrine structures (central diabetes insipidus, or CDI), or as a conse-

quence of kidney disease (nephrogenic diabetes insipidus, or NDI).

A DIFFERENT DIABETES

Diabetes insipidus has no relationship to the familiar and common form of DIABETES, known clinically as diabetes mellitus, which is a dysfunction of INSULIN. Diabetes insipidus is a dysfunction of ANTIDIURETIC HORMONE (ADH). To avoid confusion, doctors commonly refer to diabetes insipidus as CDI (central diabetes insipidus) or NDI (nephrogenic diabetes insipidus).

Central Diabetes Insipidus (CDI)

CDI may result from lesions (growths) that affect the function of the hypothalamus, though more commonly as a result of trauma to the region of the BRAIN where the hypothalamus and pituitary gland are located. Such trauma may as a consequence of accidental injury (TRAUMATIC BRAIN INJURY), STROKE, or surgery. The hypothalamus may release inadequate amounts of ADH or the pituitary gland may fail to respond. CDI may also occur when an ADENOMA (noncancerous tumor) grows in the posterior lobe of the pituitary gland and inhibits ADH secretion.

Nephrogenic Diabetes Insipidus (NDI)

In severe kidney disease or RENAL FAILURE the kidneys themselves do not respond to ADH. This leaves the kidneys unable to concentrate the urine. They consequently pass into the urine as much water as passes through them in the blood. Medications that interfere with kidney function may cause NDI. Lithium, taken to treat BIPOLAR DISORDER, and the ANTIBIOTIC MEDICATIONS demeclocycline and amphotericin B, are the most common culprits when NDI is DRUG induced.

Symptoms and Diagnostic Path

Whether central or nephrogenic, diabetes insipidus symptoms are the same. They are

- extreme thirst (called polydipsia) and often a craving for ice water
- frequent urination (called polyuria), including through the night (NOCTURIA)

It is not uncommon for a person who has diabetes insipidus to drink and urinate up to 20 liters or more every 24 hours. When symptoms develop gradually and water intake keeps pace with urination, the person may not experience the symptoms as unusual events. Diabetes insipidus results in health complications (such as electrolyte imbalance) only when the person is unable to match fluid input and output. The diagnostic path is primarily clinical (based on symptoms) with a water deprivation test to confirm the diagnosis. For this test, the person remains under continuous medical observation while consuming no water. Hourly urine tests measure the concentration of the urine. In a healthy person the urine becomes increasingly concentrated with restricted fluid consumption. In diabetes insipidus the urine remains dilute.

Because excessive thirst and urination are also symptoms of diabetes mellitus, the endocrinologist is likely to conduct blood tests to measure blood GLUCOSE and INSULIN levels. The endocrinologist may also choose to conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) or COMPUTED TOMOGRAPHY (CT) SCAN to identify traumatic injury or tumors in CDI.

Treatment Options and Outlook

Treatment targets any identified underlying cause. Thiazide diuretic medications, which ordinarily increase urination, have the opposite effect in both CDI and NDI because of their actions on the kidneys. HORMONE THERAPY with medications such as desmopressin or lypressin nasal spray is usually effective for CDI. Even when the person is able to maintain fluid balance, it is important to treat diabetes insipidus because the untreated condition results in kidney damage over time. Treatment minimizes or eliminates symptoms for most people.

Risk Factors and Preventive Measures

The primary risk factor for CDI is head trauma, in which case early intervention and treatment are most effective. Chronic kidney disorders such as POLYCYSTIC KIDNEY DISEASE are commonly the cause of NDI. Appropriately treating these disorders mitigates the NDI. It is important for people who have CDI or NDI to drink enough water to remain hydrated, to prevent complications arising from electrolyte imbalance.

See also HYPERCALCEMIA; HYPOKALEMIA; HYPONATREMIA; LESION; SARCOIDOSIS; SICKLE CELL DISEASE.

dopamine A peptide the adrenal medulla of the ADRENAL GLANDS, the HYPOTHALAMUS, and other structures in the BRAIN produce. Dopamine functions in the body as a HORMONE, when synthesized by the adrenal medulla, and as a NEUROTRANSMITTER when synthesized by brain structures or NERVE cells. NOREPINEPHRINE is a dopamine precursor (substance the body uses as the basis for dopamine synthesis).

Hormonal dopamine, also called PROLACTIN release–inhibiting factor (PRIF), is an inhibitory hormone that acts to prevent the release of the pituitary hormone prolactin. Dopamine also has less pronounced inhibitory action for FOLLICLE-STIMULATING HORMONE (FSH), LUTEINIZING HORMONE (LH), and THYROID-STIMULATING HORMONE (TSH). The hypothalamus directs the adrenal medulla to release dopamine through the neurotransmitter acetylcholine. As a neurotransmitter, dopamine is critical to voluntary MUSCLE control and movement, cognitive function, mood, emotion, and perceptions of pleasure. Dopamine appears to play a key role in ADDICTION such as to NARCOTICS and NICOTINE (cigarette smoking).

Dopamine is also a pharmaceutical DRUG used to treat CARDIAC ARREST and cardiovascular SHOCK. When injected intravenously to establish dopamine levels higher than normal in the bloodstream, dopamine constricts (narrows) peripheral BLOOD vessels to direct more blood to critical organs, intensifies the force of the HEART's contractions to increase the amount of blood the heart pumps, and increases the HEART RATE. The dopamine precursor levodopa is a treatment for PARKINSON'S DISEASE (a degenerative neurologic disorder that results from inadequate dopamine production in the sections of the brain that control movement).

For further discussion of dopamine within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also EPINEPHRINE.

endocrine gland A structure, sometimes called a ductless gland, within the body that produces chemicals, called hormones, it secretes directly into the bloodstream. Hormones influence the function of cells that contain receptors for them. The PITUITARY GLAND, ADRENAL GLANDS, and THYROID GLAND are examples of endocrine glands. An exocrine gland, by contrast, secretes the chemicals it produces into ducts (specialized channels) for release into body structures. The SALIVARY GLANDS and SWEAT GLANDS are examples of exocrine glands. The KIDNEYS, gastrointestinal tract, and PLACENTA in a pregnant woman also contain endocrine structures.

Three mechanisms can trigger endocrine activity. They are

- humoral, in which the endocrine system responds to chemicals in the bloodstream such as calcium (triggering CALCITONIN release from the thyroid gland or PARATHYROID HORMONE from the PARATHYROID GLANDS)
- hormonal, in which the hormones from one endocrine gland direct activity from other endocrine glands such as the STRESS RESPONSE HORMONAL CASCADE
- neurologic, in which NERVE impulses stimulate endocrine action such as from the HYPOTHALAMUS to the posterior lobe of the pituitary gland

Sometimes the neurologic system and the endocrine system secrete the same chemicals, such as EPINEPHRINE and NOREPINEPHRINE. When endocrine structures synthesize these chemicals, they are hormones and they travel to their target cells through the blood circulation. When the neurologic system synthesizes these structures, they are neurotransmitters, and they travel to their target cells through interstitial fluid (fluid between cells). Neurotransmitters travel to their destinations, elicit reactions, and dissipate more rapidly than hormones.

THE ENDOCRINE GLANDS

ADRENAL GLANDS	HYPOTHALAMUS	ISLETS OF LANGERHANS
OVARIES	PARATHYROID GLANDS	PINEAL GLAND
PITUITARY GLAND	PLACENTA	TESTES
THYMUS	THYROID GLAND	

For further discussion of the endocrine glands within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also DIGESTIVE HORMONES; NEUROTRANSMITTER.

epinephrine A chemical the adrenal medulla of the ADRENAL GLANDS and the synaptic vesicles of the NERVE endings produce. Epinephrine, also called adrenaline, functions in the body as a peptide HORMONE when synthesized by the adrenal medulla and as a NEUROTRANSMITTER when synthesized in the BRAIN or nerve endings. Among the hormones activated in the STRESS RESPONSE HORMONAL CASCADE, epinephrine

- constricts peripheral BLOOD vessels to centralize blood flow and raise BLOOD PRESSURE
- dilates bronchial structures in the LUNGS to increase air flow
- initiates rapid conversion of glycogen to GLUCOSE in the LIVER to raise the blood glucose level and increase energy to the cells
- intensifies the HEART's contractions to increase CARDIAC OUTPUT (the amount of blood the heart pumps out with each CARDIAC CYCLE)
- accelerates the HEART RATE

In the brain, epinephrine is an active and abundant neurotransmitter in numerous neurologic functions, including heightened alertness and cognitive function during stressful situations. Epinephrine is also a pharmaceutical DRUG used to treat CARDIAC ARREST and cardiovascular SHOCK. When injected intravenously to produce blood levels significantly higher than normal in the bloodstream, epinephrine causes accelerated actions such as those it initiates as an endogenous hormone in the stress response. It also stabilizes the electrical activity of the heart to normalize the heart's rhythm (antiarrhythmic). In other pharmaceutical applications epinephrine blocks the body's inflammatory response in severe allergic reactions and anaphylactic shock, and can reduce bleeding and extend the effectiveness of injected local anesthetics.

EPINEPHRINE, ADRENALINE, OR ADRENALIN?

Epinephrine, adrenaline, and Adrenalin are the same chemical. Adrenalin (no *e*) is a proprietary DRUG trademarked in the United States. Epinephrine and adrenaline designate either the endogenous chemical (HORMONE or NEUROTRANSMITTER) or the GENERIC DRUG. Only the United States uses the term *epinephrine*. Other countries follow the international standard terminology, which uses the term *adrenaline*. This is because in the United States trademark protections prevent alternate names for trademarked products that could be confused with the trademark.

For further discussion of epinephrine within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also DOPAMINE; NOREPINEPHRINE.

estrogens A collective term for the "female" sex hormones, including prohormones (chemical precursors the body converts to hormones) and metabolites (byproducts of HORMONE METABOLISM). Estrogens are among the steroid hormones the body synthesizes from cholesterol. Estrogens derive from ANDROGENS (the "male" sex hormones).

Common use applies the singular term estrogen to refer to any or all of the three endogenous (naturally occurring within the body) estrogen hormones: estradiol, estriol, and estrone. Estradiol is the most potent and most biochemically active of the estrogens. Estrone is very similar in chemical structure to estradiol though exerts a weaker response. Estriol is a metabolite of both estradiol and estrone.

In a woman's body the levels of these closely related hormones change at MENARCHE and at MENOPAUSE, and fluctuate within the menstrual cycle and with PREGNANCY. Estradiol is the predominant estrogen during the years of FERTILITY, with the less-potent estrone moving into dominance after menopause. In a man's body estrogen levels remain fairly constant. The HYPOTHALAMUS's secretion of GONADOTROPIN-RELEASING HORMONE (GNRH) regulates the hormonal cascade for production and release of the estrogens. In women this cascade is cyclic, establishing the monthly menstrual cycle during the four decades or so a woman is fertile.

Men and women alike have estrogens (just as both sexes also have androgens). The OVARIES in women, the TESTES in men, and the adrenal cortex of the ADRENAL GLANDS in men and women synthesize (produce) most of the estrogens in the BLOOD circulation. During pregnancy the PLACENTA produces estrogens as well. Adipose (fat) cells and the LIVER in both sexes, and the breasts in women, also synthesize small amounts of estrogens.

In women the estrogens establish secondary sex characteristics and fertility, and maintain pregnancy. The estrogens are essential in both sexes for cholesterol metabolism, BONE calcium content and density, thyroid function, SKIN health, and collagen maintenance. The estrogens also have roles in mood and emotion, probably in both men and women though more pronounced in women because estrogen levels fluctuate with the menstrual cycle.

Various endocrine disorders may result in estrogen levels that are too high or too low, with consequences for fertility in women and for cholesterol metabolism in men and women. Doctors use pharmaceutical preparations of estrogens and estrogen analogs (drugs that bind with estrogen receptors though do not have estrogen activity) for a diverse array of therapeutic applications including CONTRACEPTION (birth control pills), treatment for HORMONE-DRIVEN CANCERS (notably PROSTATE

CANCER) in men, OSTEOPOROSIS and BREAST CANCER prevention in women (estrogen analogs), and fertility treatments in women.

Estrogen products were a mainstay of therapy (alone or in combination with PROGESTERONE) to relieve the discomforts of menopause for much of the latter half of the 20th century. Research in the early 2000s demonstrated significant risks with routine hormone replacement therapy (HRT), however, resulting in a change in medical practice to use such products within narrow therapeutic guidelines and for the shortest amount of time possible to achieve a therapeutic result.

For further discussion of estrogen within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also CHLOASMA; ENDOMETRIAL CANCER; FOLLICLE-STIMULATING HORMONE (FSH); GYNECOMASTIA; HORMONE THERAPY; HYPOGONADISM; HYPOTHYROIDISM; INFERTILITY; LUTEINIZING HORMONE (LH); MENSTRUATION; PHYTOESTROGENS; POLYCYSTIC OVARY SYNDROME (PCOS); TESTOSTERONE; THYROID GLAND.

euthyroid sick syndrome A circumstance in which BLOOD tests show irregular thyroid HORMONE levels in the blood but hypothalamic, pituitary, and thyroid functions are all normal. Euthyroid sick syndrome typically accompanies a severe acute illness or chronic condition. Many medications interfere with thyroid function, altering thyroid hormone levels in the blood. Because the body experiences significant physiologic stress with severe illness, many of the body's natural hormonal responses have the consequence of altering thyroid hormone levels.

Typically there are no symptoms of hypothyroidism with euthyroid sick syndrome, though the symptoms of the health condition may make this difficult to assess. Declining thyroid hormone levels, measured through blood tests, provide important insight into the overall crisis state the body is experiencing. There appears to be no benefit in treating euthyroid sick syndrome with replacement thyroid hormones, so most doctors choose a course of watchful waiting in regard to thyroid function and focus therapeutic efforts on the causative condition. Thyroid hormone levels gradually return to normal as the person recovers from the underlying acute illness or when the chronic condition improves.

CONDITIONS THAT MAY RESULT IN EUTHYROID SICK SYNDROME

BONE MARROW TRANSPLANTATION	BURNS
CANCER	CARDIOMYOPATHY
chronic CIRRHOSIS	CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)
DIABETES	GLOMERULONEPHRITIS
GLOMERULOSCLEROSIS	HEART FAILURE
INFLAMMATORY BOWEL DISEASE (IBD)	major surgery
ISCHEMIC HEART DISEASE (IHD)	ORGAN TRANSPLANTATION
MYOCARDIAL INFARCTION	POLYGLANDULAR DEFICIENCY SYNDROME
PANCREATITIS	severe GASTROENTERITIS
RENAL FAILURE	major trauma
SARCOIDOSIS	
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	

See also GOITER; HYPERTHYROIDISM; THYROID GLAND.

follicle-stimulating hormone (FSH) A peptide HORMONE the anterior lobe of the PITUITARY GLAND secretes in response to stimulation from the HYPOTHALAMUS's release of GONADOTROPIN-STIMULATING HORMONE (GNHR). In women, FSH stimulates the follicles in the OVARIES to bring eggs (OVA) to maturity. In men, FSH stimulates growth of cells in the TESTES and synthesis of proteins necessary to support spermatogenesis (production of SPERM). The actions of FSH closely intertwine with those of another pituitary hormone, LUTEINIZING HORMONE (LH). Pituitary tumors can interfere with FSH synthesis, causing the pituitary gland to produce inadequate or excessive amounts. Extended use of ANABOLIC STEROIDS AND STEROID PRECURSORS suppresses both GnRH and FSH (as well as LH), resulting in symptoms of HYPOGONADISM that are most pronounced in men though can occur in women as well. HORMONE THERAPY as treatment for PROSTATE CANCER has the same effect.

For further discussion of FSH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ANDROGENS; ANTIDIURETIC HORMONE (ADH); CRYPTORCHIDISM; ESTROGENS; FERTILITY; GROWTH HORMONE (GH); KLINEFELTER'S SYNDROME; INFERTILITY; OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (TSH); TURNER'S SYNDROME.

G

gastric inhibitive polypeptide (GPI) See DIGESTIVE HORMONES.

gastrin See DIGESTIVE HORMONES.

glucagon A peptide HORMONE the alpha cells of the ISLETS OF LANGERHANS produce in response to low blood GLUCOSE levels (humoral regulation). Intense physical exercise also causes the release of glucagon into the bloodstream. Glucagon stimulates the LIVER to convert glycogen (a storage form of glucose) into glucose to raise the level of glucose in the BLOOD. Glucagon opposes the action of INSULIN (which stimulates glucose use or conversion to glycogen to decrease blood glucose levels). High blood glucose levels inhibit glucagon production as does release of SOMATOSTATIN, another peptide hormone synthesized by the HYPOTHALAMUS, gastrointestinal tract, and delta cells of the islets of Langerhans. Glucagon is also available as a pharmaceutical DRUG used to treat HYPOGLYCEMIA (low blood glucose) and insulin shock.

For further discussion of glucagon within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also DIABETES; DIGESTIVE HORMONES; LIVER; METABOLISM.

glucose A simple sugar molecule (monosaccharide) that is the primary energy source for most cells in the body. The body metabolizes (breaks down) carbohydrates, which enter the body from the gastrointestinal tract, into glucose. The body requires a fairly narrow but constant level of available glucose circulating in the BLOOD at all times (70 to 110 milligrams of glucose per deciliter of blood). Glucose and two hormones the ISLETS OF LANGERHANS in the PANCREAS produce, INSULIN and GLUCAGON, function in synchronization and opposition to maintain this level.

Rising glucose levels in the blood signal the islets of Langerhans to secrete insulin. The insulin binds with receptors on cell membranes, enabling glucose to enter the cells. Within the cell the glucose causes a series of biochemical actions that result in the formation of adenosine triphosphate (ATP), which fuels cellular METABOLISM. Insulin (in coordination with CORTISOL) also stimulates the LIVER to extract excess glucose from the blood and convert it to glycogen, a storage form of glucose the liver then deposits within its tissues as well as within MUSCLE tissue throughout the body. When the blood glucose level drops, the islets of Langerhans release glucagon, a hormone that causes the liver to convert glycogen back to glucose and release it into the blood circulation. Glucagon also stimulates DIGESTIVE HORMONES and enzymes that result in the sensation of hunger, encouraging food intake that can more rapidly replenish the body's glucose supply.

FASTING BLOOD GLUCOSE LEVELS

Health Condition	Milligrams of Glucose per Deciliter of Blood
hypoglycemia	< 50
normal	70–110
hyperglycemia (prediabetes)	111–125
DIABETES	> 126

See also CELL STRUCTURE AND FUNCTION.

goiter Swelling and enlargement of the THYROID GLAND. Most often goiter occurs as a symptom of thyroid dysfunction though can develop when thyroid function is normal, such as sometimes

occurs as a consequence of PREGNANCY (when the body's need for thyroid hormones increases) or in EUTHYROID SICK SYNDROME (when a health crisis disrupts the entire endocrine matrix). A goiter may cause uniform enlargement of the thyroid gland (diffuse goiter) or isolated enlargement (nodular goiter). Though typically a goiter is visible on the front of the neck, occasionally a nodular goiter forms on the back of a thyroid lobe, near the end, pressuring the airway. Among the numerous causes of goiter are

- iodine deficiency
- HYPOTHYROIDISM (underactive thyroid)
- HYPERTHYROIDISM (overactive thyroid), including GRAVES'S DISEASE
- THYROIDITIS (INFLAMMATION of the thyroid gland)
- radiation exposure (such as from RADIATION THERAPY to treat CANCER of the larynx, MOUTH, or upper chest)
- thyroid nodules (noncancerous growths)
- THYROID CANCER

Hypothyroidism, hyperthyroidism, and thyroiditis are the most common causes of diffuse goiter. Thyroid nodules, which are fairly common, and thyroid cancer, which is relatively uncommon, are more likely to cause nodular goiter. Iodine deficiency is rare in the United States because most table salt is iodized. Symptoms of goiter may include

- visible swelling on one side or both sides of the neck
- palpable lump in the neck, especially when swallowing
- difficulty swallowing or the sensation of something being stuck in the THROAT
- difficulty breathing, usually with exhalation

Many people also have symptoms of hypothyroidism or hyperthyroidism, when either condition is the cause of the goiter. The diagnostic path includes blood tests to measure the level of thyroid hormones, ULTRASOUND of the neck, and often a radionuclide scan or COMPUTED TOMOGRAPHY (CT) SCAN. Treatment depends on the findings and the extent to which symptoms interfere with functions such as swallowing or BREATHING. If surgery to remove the thyroid gland is necessary (thyroidectomy), the person will need to take lifelong thyroid supplementation (thyroid HORMONE THERAPY). Endocrinologists typically take an approach of watchful waiting with a goiter that causes no symptoms and does not affect thyroid function (thyroid hormone levels are normal).

See also AUTOIMMUNE DISORDERS; LYMPHOMA; THYROID NODULE.

gonadotropin-releasing hormone (GnRH) A peptide HORMONE, also called luteinizing hormone-releasing hormone (LHRH), the HYPOTHALAMUS produces to stimulate the anterior lobe of the PITUITARY GLAND to synthesize and release LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH). LH and FSH in turn stimulate the gonads, or sex glands, to produce their respective hormones. In women the effect stimulates the OVARIES to produce ESTROGENS and PROGESTERONE, and in men stimulates the TESTES in men to produce TESTOSTERONE. When these sex hormones reach certain levels in the bloodstream the hypothalamus stops secreting GnRH, and the gonadotropic cascade stops—a negative-feedback loop. In women these levels fluctuate according to the menstrual cycle. Other hormones may also influence the release of GnRH.

Doctors sometimes use a pharmaceutical preparation of GnRH, called a GnRH analog, to treat ENDOMETRIOSIS. Because its chemical composition is nearly identical to that of endogenous GnRH, a GnRH analog binds with GnRH receptors to block endogenous GnRH binding. This prevents the release of LH and FSH, and consequently suppresses the menstrual cycle and OVULATION.

For further discussion of GnRH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ANTIDIURETIC HORMONE (ADH); GROWTH HORMONE (GH); INHIBIN; MENSTRUATION; OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (THS).

Graves's disease An autoimmune disorder in which the body produces antibodies that attack the THYROID GLAND, producing symptoms of HYPERTHYROIDISM (overactive thyroid gland). The most

common cause of hyperthyroidism, Graves's disease affects seven times as many women as men and is most frequent among women between the ages of 30 and 60. Graves's disease is more likely to occur among people who have other AUTOIMMUNE DISORDERS, notably type 1 DIABETES, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and POLYGLANDULAR DEFICIENCY SYNDROME.

In health the HYPOTHALAMUS, PITUITARY GLAND, and thyroid gland work in synchronization to maintain an appropriate balance of thyroid hormones, which regulate METABOLISM, in the BLOOD circulation. Low blood levels of the major thyroid hormones TRIIODOTHYRONINE (T_3) and THYROXINE (T_4) signal the hypothalamus to produce THYROTROPIN-RELEASING HORMONE (TRH). TRH in turn stimulates the pituitary gland to secrete THYROID-STIMULATING HORMONE (TSH). TSH binds with TSH receptors on the cells of the thyroid gland, activating synthesis of T_3 and T_4. When T_3 and T_4 reach appropriate levels in the bloodstream, the hypothalamus stops producing TRH and the thyroid hormone cascade ends.

The antibodies the IMMUNE SYSTEM produces in Graves's disease, called thyroid-stimulating immunoglobulins (TSIs), continuously stimulate the TSH receptors in the thyroid gland, falsely signaling that blood T_3 and T_4 levels are too low. The thyroid gland responds by increasing synthesis of these hormones. It is an overproduction, however. TSH and TRH levels fall as they should but thyroid hormone production continues in the thyroid gland, resulting in hyperthyroidism. Graves's disease accounts for about 70 percent of hyperthyroidism in the United States.

A serious corollary condition is GRAVES'S OPHTHALMOPATHY, in which the excessive thyroid hormones cause swelling in and around the structures of the eyes. Graves's ophthalmopathy is often the earliest indication of Graves's disease and can result in permanent damage to the eyes, including loss of vision. The characteristic symptom of Graves's ophthalmopathy is EXOPHTHALMOS (bulging eyes, also called poptosis). Some endocrinologists believe Graves's ophthalmopathy is a distinct autoimmune disease process separate from Graves's disease, as it may exist without apparent hyperthyroidism or develop years to decades before or after hyperthyroidism manifests.

Symptoms and Diagnostic Path

The symptoms of Graves's disease are those of hyperthyroidism and may include symptoms of Graves's ophthalmopathy as well. These symptoms are

- PALPITATIONS
- weight loss
- heat intolerance
- difficulty concentrating
- irritability, anxiety, and insomnia (difficulty sleeping)
- bulging eyes (poptosis), "lid lag" (delay in the eyelid's movement when the EYE moves downward), and vision disturbances (Graves's ophthalmopathy)

The diagnostic path includes blood tests to measure thyroid hormones (typically T_3, T_4, and TSH) and the presence of TSIs. The former establish hyperthyroidism; the latter confirms the diagnosis of Graves's disease.

Treatment Options and Outlook

Treatment targets disabling the thyroid gland's ability to synthesize thyroid hormones. Because Graves's disease is a progressive autoimmune disorder, endocrinologists tend to opt for permanent therapies such as radioactive iodine (^{131}I) to destroy thyroid tissue so it cannot produce thyroid hormones. One consequence of this approach is that the destruction of the thyroid gland results in permanent hypothyroidism and makes necessary lifelong HORMONE THERAPY with thyroid hormone supplements. Thyrotoxic medications such as methimazole and propylthiouracil (PTU), though effective in other forms of hyperthyroidism, are less successful because the autoimmune response continues.

Risk Factors and Preventive Measures

Women who have other autoimmune disorders have increased risk for Graves's disease. For them, regular blood tests to measure thyroid hormones can help detect the condition early. Routine ophthalmologic examinations can detect Graves's ophthalmopathy, which may develop even with treatment for Graves's disease, before it causes

permanent damage to the eyes and vision. No known preventive measures exist for Graves's disease.

See also IMMUNE RESPONSE; LYMPHOCYTE; THYROIDITIS; THYROID STORM; VISION HEALTH.

growth hormone (GH) A peptide HORMONE the PITUITARY GLAND produces in response to secretion of GROWTH HORMONE–RELEASING HORMONE (GHRH) by the HYPOTHALAMUS. GH affects growth directly by initiating an increase in cell division and indirectly by stimulating the production of insulinlike growth factors (IGFs), proteins that affect cell METABOLISM and other functions. GH levels are highest in childhood, then taper off in early adulthood to maintain a stable level. GH remains essential in adulthood to maintain appropriate cell metabolism, notably in BRAIN, MUSCLE, and fat cells. GROWTH HORMONE DEFICIENCY in childhood results in stunted growth, and in adulthood can result in diminished cognitive function, decreased muscle mass, and increased body fat. Some researchers believe the decline in GH in adulthood contributes to the aging process, though the mechanisms through which this occurs remain unknown. Excessive GH secretion, such as may occur with a pituitary ADENOMA, results in ACROMEGALY.

For further discussion of growth hormone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (SCTH); ANABOLIC STEROIDS AND STEROID PRECURSORS; ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); HUMAN GROWTH HORMONE (HGH) SUPPLEMENT; LUTEINIZING HORMONE (LH); OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (TSH).

growth hormone deficiency An endocrine disorder in which the anterior lobe of the PITUITARY GLAND produces an inadequate amount of GROWTH HORMONE (GH). GH is fundamental for proper growth and development in childhood and remains essential for appropriate metabolic function in adulthood. In childhood GH binds to receptors in BONE cells that increases the rate at which they divide, causing bone growth that results in increased height. In adulthood GH deficiency can affect cognitive functions and memory, body mass and fat distribution, and numerous aspects of cell METABOLISM.

It is important to distinguish between abnormal growth and a child who is simply short in stature. The average rate of growth for children is about two inches a year. Many factors influence a child's ultimate height. Indications in addition to short stature that a child may have GH deficiency include accumulations of body fat in the abdomen and the face (giving a rounded, chubby appearance), delayed eruption of TEETH, and in an older child, delayed PUBERTY. The diagnostic path includes

- BLOOD tests to measure thyroid hormones (HYPOTHYROIDISM can cause slowed growth) and insulinlike growth factors (IGFs)
- measuring height and weight over a period of time to detect growth patterns
- X-rays and sometimes COMPUTED TOMOGRAPHY (CT) SCAN to evaluate bone structure
- a GROWTH HORMONE–RELEASING HORMONE (GHRH) challenge test to measure the ability of the pituitary gland to respond to stimulation by GHRH

Treatment for confirmed GH deficiency in children is injections of recombinant human growth hormone (hGH), a genetically engineered substance that has the precise configuration of endogenous GH, continued until the child reaches appropriate growth. Some people develop antibodies to the recombinant hGH, decreasing its effectiveness. When the pituitary gland is congenitally absent (a birth defect) or permanently damaged, long-term hGH therapy may be necessary. Whether treatment continues into adulthood depends on symptoms and the cause of the deficiency. Doctors do not agree on the definition or the need for treatment of adult growth hormone deficiency that does not begin in childhood.

See also ACROMEGALY; ADRENAL INSUFFICIENCY; HUMAN GROWTH HORMONE (HGH) SUPPLEMENT; POLYGLANDULAR DEFICIENCY SYNDROME; TURNER'S SYNDROME.

growth hormone–releasing hormone (GHRH) A peptide HORMONE the HYPOTHALAMUS produces to stimulate the PITUITARY GLAND to synthesize and

release GROWTH HORMONE (GH). The secretion of GHRH initiates a cascade of chemical activity that results in intensified cell METABOLISM and processes that promote cell division and the growth of body tissues and structures. The hormone SOMATOSTATIN, which the hypothalamus and the delta cells of the ISLETS OF LANGERHANS produce, provides the stimulus for the hypothalamus to stop releasing GHRH. Multiple factors regulate the balance between GHRH and somatostatin.

For further discussion of GHRH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ACROMEGALY; ADRENOCORTICOTROPIN HORMONE (ACTH); ANABOLIC STEROIDS AND STEROID PRECURSORS; ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE DEFICIENCY; LUTEINIZING HORMONE (LH); OXYTOCIN; PROLACTIN; THYROID-STIMULATING HORMONE (TSH).

H

Hashimoto's disease See THYROIDITIS.

hemochromatosis A genetic disorder in which the gastrointestinal tract absorbs too much iron into the bloodstream. The BLOOD deposits the excess iron in various tissues and organs, where it accumulates and eventually causes damage. Common sites for deposits include the HEART, causing HEART FAILURE, PANCREAS, causing DIABETES, and LIVER, causing CIRRHOSIS and LIVER FAILURE. Though hemochromatosis is congenital (present from birth), most people do not experience consequences or symptoms until midlife when enough iron has accumulated in the organs to affect their functions.

Health experts believe hemochromatosis is far more common than the number of people diagnosed with the condition suggests. Women may not show symptoms until 10 or more years after MENOPAUSE because the bleeding associated with MENSTRUATION reduces blood iron concentrations, serving as a natural therapy for the hemochromatosis. Researchers have identified several GENE mutations that can cause hemochromatosis. The most common mutations are those involving the HFE gene that regulates gastrointestinal iron absorption. Researchers have designated them C282Y and H63D, and they account for about 85 percent of diagnosed hemochromatosis in the United States.

Symptoms and Diagnostic Path

Doctors often detect hemochromatosis during evaluation for other health concerns, when blood tests show higher than normal HEMOGLOBIN or iron levels. The symptoms of hemochromatosis result from damage to organs and structures where iron deposits accumulate and often take the form of fairly advanced disease states by the time of detection. General symptoms may include

- JOINT PAIN (the most common symptom)
- fatigue and lethargy
- abdominal discomfort or PAIN

The excessive iron in the body may also interfere with FERTILITY (causing early menopause in women) and LIBIDO (sex drive). The diagnostic path includes general blood tests to measure hemoglobin, hematocrit, red blood cells, and specialized blood tests that measure iron. The most commonly used are

- transferrin saturation, which measures how much iron the hemoglobin carries (protein saturation)
- total iron binding capacity (TIBC), which measures the capacity of the hemoglobin to transport iron
- serum ferritin, which measures the iron the liver contains

Elevated results in any of these tests suggests hemochromatosis. Further blood analysis to detect the HFE gene mutation and liver biopsy are the final steps in the diagnostic path and provide a definitive diagnosis.

Treatment Options and Outlook

Treatment for hemochromatosis is phlebotomy, the withdrawal of blood a pint at a time. Initial treatment may take place several times a week until blood levels of iron return to normal. Most people then require phlebotomy sessions only once every two to four months, though lifelong treatment is necessary. Treatment also targets any

health conditions that have developed as a consequence of iron deposits, such as heart disease or diabetes. The damage iron deposits cause is irreversible, though once treatment begins most secondary conditions improve.

DONATING BLOOD

Some BLOOD banks and blood collection centers accept blood withdrawn as treatment hemochromatosis for donation and use it to produce blood products. As blood products are limited and sometimes scarce, it is worthy for people who are receiving therapeutic phlebotomy for hemochromatosis to look for centers who will accept their blood for such use. Otherwise the center discards the blood.

Risk Factors and Preventive Measures

Because hemochromatosis is hereditary, the key risk for developing it is family history. Doctors have only recently recognized the potentially widespread existence of hemochromatosis, however; and many family medical histories make no reference to the condition. People who have family histories for early-onset liver disease, heart disease, or diabetes should have basic blood tests for iron levels included with their routine medical examinations as a screening precaution. Early diagnosis and treatment prevent most of the complications that can develop and minimize the severity of the condition and its affect on health.

See also BLOOD DONATION; PHENYLKETONURIA (PKU); WILSON'S DISEASE.

hirsutism Excessive growth of body HAIR in a male pattern, typically involving the face, chest, back, arms, and legs. The hair follicles on these SKIN surfaces are sensitive to TESTOSTERONE and other ANDROGENS ("male" hormones), the hormones that stimulate hair growth in both men and women. Though hirsutism affects men and women, it is especially a concern for women for clinical as well as cosmetic reasons. Hirsutism may result from the hair follicles being overly sensitive to the effects of androgens (with normal levels of androgens in the BLOOD) or an excess of androgens in the blood circulation.

In the latter circumstance, researchers believe the culprit is overactivity of an enzyme, 5-alpha reductase, that converts testosterone to dihydrotestosterone, the androgen form that stimulates hair growth. Excessive blood levels of testosterone may result from androgen-secreting tumors that form in the OVARIES or the adrenal cortex of the ADRENAL GLANDS, the two primary sources of endogenous testosterone. Women athletes who use ANABOLIC STEROIDS AND STEROID PRECURSORS may also develop hirsutism. INSULIN RESISTANCE and POLYCYSTIC OVARY SYNDROME (PCOS), existing independently or as constituents of INSULIN resistance, are strongly associated with hirsutism in women. In some situations the endocrinologist cannot determine a definitive cause for hirsutism (idiopathic hirsutism).

The diagnostic path includes blood tests to measure hormone levels, hormonal responses, and insulin sensitivity. The precise tests depend on the findings of preliminary tests. ULTRASOUND or MAGNETIC RESONANCE IMAGING (MRI) of the ovaries or imaging procedures to visualize the adrenal glands may identify any tumors. Treatment depends on any identified cause and may combine HORMONE THERAPY to suppress androgen production or binding with cosmetic therapies to remove or minimize excessive hair. The most commonly used hormone therapy is the oral contraceptive (birth control pill), which regulates the hormonal cycle of the ovaries. The endocrinologist may prescribe other hormone products, such as CORTICOSTEROID MEDICATIONS, to suppress the HORMONE production of the adrenal cortex. These methods are effective for many though not all people who have hirsutism. Cosmetic approaches include electrolysis or laser therapy to permanently destroy hair follicles. Shaving and chemical depilatories (hair removers) are sometimes effective though require frequent use. Hirsutism can be emotionally difficult for those who have it, especially women, though men as well may find the condition distressing.

See also CONTRACEPTION; GENETIC DISORDERS; PORPHYRIA.

hormone A chemical that travels through the blood circulation and influences the functions of cells within the body. The body produces dozens of hormones of two primary chemical forms, peptides and steroids. A hormone affects only the cells that have receptors for it, and only when it binds

to those receptors. A receptor is somewhat like an outlet that has a unique configuration. The hormone for which the receptor is sensitive matches that configuration, forming a chemical "lock" between the hormone molecule and the cell. Through such binding hormones cause chemical changes within the cell that may activate enzymes or alter the cell's genetic encoding by creating new proteins (called genetic transcription). Each hormone has unique receptors. Many cells have receptors only for certain hormones, eliciting specific and narrowly focused changes. Only cells in the TESTES and OVARIES, for example, have receptors for FOLLICLE-STIMULATING HORMONE (FSH) and LUTEINIZING HORMONE (LH). Some hormones, such as GROWTH HORMONE (GH), have receptors in all cells, in which case the hormone has widespread actions.

Some hormones stimulate and others inhibit activity. Most hormonal responses occur in cascades, with multiple activities resulting from the hormone's release. For example, the HYPOTHALAMUS releases GROWTH HORMONE–RELEASING HORMONE (GHRH), which stimulates the PITUITARY GLAND to release GH. Growth hormone initiates metabolic changes within some cells, such as the BONE and MUSCLE, and also activates the production of insulinlike growth factors (IGFs) that induce metabolic activity in other cells.

Peptide Hormones

Peptide hormones consist of amino acid chains and are the most abundant form of endogenous hormone. Scientists further define peptide hormones as small peptide (fewer than 10 amino acids), polypeptide (more than 10 and fewer than 100 amino acids), or protein (100 or more amino acids), depending on the length and configuration of the amino acid chain. These distinctions influence the hormone's mechanisms of action, stability, and receptor binding. Most of the body's hormones are peptide hormones.

Peptide hormones are water soluble and travel through the bloodstream attached to protein molecules called protein carriers. These larger structures keep the hormone intact during transit. Most peptide hormones cannot penetrate the wall of the cell. Instead, they bind with protein receptors on the cell's surface (also called the plasma membrane). The binding causes a chemical reaction that activates proteins within the cell that then carry the hormone's message within the cell, indirectly influencing cell activity. Among the exceptions are the thyroid hormones, which do cross the cell membrane to bind with receptors in the cell nucleus and directly influence the cell's activity.

PEPTIDE HORMONES

ANTIDIURETIC HORMONE (ADH)	CALCITONIN
cholecystokinin (CCK)	CHORIONIC GONADOTROPIN
CORTICOTROPIN-RELEASING HORMONE (CRH)	enterogastrone
gastric inhibitive polypeptide (GPI)	FOLLICLE-STIMULATING HORMONE (FSH)
GLUCAGON	gastrin
GROWTH HORMONE (GH)	GONADOTROPIN-RELEASING HORMONE (GNRH)
GROWTH HORMONE–RELEASING HORMONE (GHRH)	INHIBIN
LUTEINIZING HORMONE (LH)	INSULIN
motilin	MELATONIN
PARATHYROID HORMONE	OXYTOCIN
RELAXIN	PROLACTIN
secretin	RENIN
THYROID-STIMULATING HORMONE (TSH)	SOMATOSTATIN
THYROXINE (T_4)	THYROTROPIN-RELEASING HORMONE (TRH)
vasoactive intestinal peptide (VIP)	TRIIODOTHYRONINE (T_3)

Steroid Hormones

Steroid hormones are lipid structures that derive from cholesterol. Scientists further define steroid hormones as corticosteroids (glucocorticoids and mineralocorticoids), sex steroids (ANDROGENS, ESTROGENS, PROGESTERONE), and vitamin D derivatives. Like peptide hormones, steroid hormones bind to protein carriers to transport them through the bloodstream to their target cells. Steroid hormones penetrate the wall of the cell to bind with receptors (specialized proteins) within the cytoplasm or cell nucleus to directly alter the cell's activity. Steroid hormones elicit genetic transcription responses in the cells that contain their receptors.

ENDOGENOUS STEROID HORMONES

ALDOSTERONE	CORTISOL	ESTROGENS
PROGESTERONE	TESTOSTERONE	vitamin D

Pharmaceutical Hormones

Most of the major endocrine hormones are available as purified extracts or synthesized products for therapeutic supplementation or replacement therapy. Endocrinologists and other doctors prescribe pharmaceutical conditions to treat a wide range of endocrine disorders such as ADDISON'S DISEASE, HYPOTHYROIDISM, and DIABETES. Doctors may also prescribe pharmaceutical hormones for CONTRACEPTION (the birth control pill), to enhance FERTILITY, to slow or prevent OSTEOPOROSIS, and to treat HORMONE-DRIVEN CANCERS such as PROSTATE CANCER, ENDOMETRIAL CANCER, and some forms of BREAST CANCER.

Many hormone supplements are recombinant products genetically engineered in laboratories to precisely match the chemical configurations of endogenous (native to the human body) hormones. Some hormone products contain purified extracts drawn from animal sources, most commonly human (extracted from donor cadaver organs), porcine (pig) and bovine (cow). Most people can tolerate either type of supplement, though adverse reactions (including allergic responses) tend to be more common with extracts.

For further discussion of hormones within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; DIGESTIVE ENZYMES; DIGESTIVE HORMONES; ENDOCRINE GLAND; HORMONE THERAPY.

hormone therapy Treatment in which a person takes HORMONE extracts or synthetic hormones to influence the body's natural production of hormones or to replace hormones the body is no longer producing. Nearly all of the body's major hormones are available as purified extracts, laboratory-synthesized pharmaceuticals, or recombinant products. Common hormone therapy regimens include replacement supplements to treat:

- ACROMEGALY
- ADDISON'S DISEASE
- ADRENAL INSUFFICIENCY
- DIABETES
- GROWTH HORMONE DEFICIENCY
- HYPOPARATHYROIDISM
- HYPOPITUITARISM (especially following treatment for adenoma)
- HYPOTHYROIDISM

Hormone therapy may also be a treatment approach for HORMONE-DRIVEN CANCERS such as PROSTATE CANCER, some BREAST CANCERS, and ENDOMETRIAL CANCER (cancer of the UTERUS). Doctors may also prescribe short-term hormone replacement therapy (HRT) for moderate to severe symptoms related to MENOPAUSE. FERTILITY treatments typically involve hormone therapy to stimulate OVULATION in women or SPERM production in men.

CHANGE IN HRT PRACTICES

For the latter half of the 20th century doctors routinely prescribed moderate doses of ESTROGENS and progestins for women going through and beyond MENOPAUSE, based on the presumption that such hormone replacement therapy (HRT) protected women from heart disease and OSTEOPOROSIS. Several large studies in the early 2000s disproved this premise, establishing concern that routine HRT increased the risk for heart disease as well as HORMONE-DRIVEN CANCERS. Doctors now prescribe small doses of these hormones for short periods of time and only for women who are experiencing moderate to severe symptoms such as hot flashes and sleep disturbances.

See also CANCER TREATMENT OTIONS AND DECISIONS; OSTEOPOROSIS.

hydrocortisone See CORTISOL.

hyperaldosteronism A condition, also called aldosteronism, in which the adrenal cortex of the ADRENAL GLANDS produces excessive ALDOSTERONE. This causes the KIDNEYS to withhold higher amounts of sodium in the BLOOD and pass into the URINE greater amounts of potassium, which consequently draws greater amounts of water into the blood. The aldosterone also causes the peripheral arterioles (tiny arteries in the CAPILLARY BEDS) to constrict. The combined effect is elevated BLOOD PRESSURE along with an imbalance between sodium and potassium. This imbalance causes disturbances

of the HEART's rhythm (ARRHYTHMIA) that can have serious consequences.

The most common cause of hyperaldosteronism is an ADENOMA (a noncancerous tumor) that grows in the zona glomerulosa, the region of the adrenal cortex that produces aldosterone. Symptoms may appear gradually or rapidly depending on the location and rate of growth of the adenoma. In addition to HYPERTENSION (high blood pressure) and arrhythmias, symptoms may include HEADACHE and fatigue. Some people also experience weakness or dizziness, a potential consequence of arrhythmias.

The diagnostic path includes blood tests to measure the levels of aldosterone and potassium, imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to determine the presence of an adrenal tumor, and ELECTROCARDIOGRAM (ECG) to detect and evaluate any arrhythmias. Treatment is surgery to remove the tumor, when possible. The endocrinologist may also prescribe medications such as the potassium-sparing diuretic spironolactone, which works by suppressing aldosterone secretion, in conjunction with a low-sodium diet to help control symptoms either in lieu of surgery or after surgery if the hypertension persists.

Hyperaldosteronism may also develop as a secondary condition resulting from severe CARDIOVASCULAR DISEASE (CVD) such as uncontrolled hypertension or HEART FAILURE. Treatment when this is the case targets the underlying condition and often also incorporates similar dietary restrictions and medications to those prescribed for primary hyperaldosteronism.

See also ADDISON'S DISEASE; ADRENAL INSUFFICIENCY; CUSHING'S SYNDROME.

hypercalcemia A circumstance of excessive calcium in the BLOOD circulation. The most common cause of hypercalcemia is HYPERPARATHYROIDISM (excessive secretion of PARATHYROID HORMONE). Other causes include HYPERTHYROIDISM (overactive THYROID GLAND), long-term therapy with lithium (treatment for BIPOLAR DISORDER) or thiazide diuretics ("water pills"), excessive vitamin D or vitamin A consumption, excessive consumption of calcium carbonate (a form of antacid often taken as a calcium supplement), and some cancers, notably metastatic BONE CANCER.

Hypercalcemia occurs when the bones release excessive calcium into the BLOOD circulation. The loss of calcium weakens the structure of the bones, causing symptoms similar to OSTEOPOROSIS such as BONE PAIN and, when calcium loss is severe, spontaneous fractures. However, hypercalcemia is likely to cause other, more apparent symptoms before the calcium loss reaches such a point.

Calcium is essential for MUSCLE contractions and for the conduction of NERVE impulses, an especially critical combination in the HEART. Hypercalcemia may cause ARRHYTHMIAS (irregularities in the HEART RATE), which are apparent with ELECTROCARDIOGRAM (ECG), and HYPERTENSION (high BLOOD PRESSURE). Hypercalcemia also often has neurologic symptoms as well, such as confusion and cognitive dysfunction, because the excessive calcium in the blood disrupts nerve communication in the BRAIN.

The diagnostic path begins with blood tests to measure calcium and parathyroid hormone levels in the blood. The doctor may conduct an ECG to evaluate any cardiovascular symptoms, and X-rays Or bone scan to assess BONE DENSITY loss or the presence of tumors, particularly in people who have or have been treated for LYMPHOMA, LEUKEMIA, MULTIPLE MYELOMA, or CARCINOMA. People who have received RADIATION THERAPY to the neck, such as to treat THYROID CANCER or HYPERTHYROIDISM, are vulnerable to parathyroid ADENOMA (noncancerous tumor of a parathyroid gland) or hyperparathyroidism.

Treatment depends on the severity of the hypercalcemia and any underlying causes. Mild to moderate hypercalcemia may improve with increased HYDRATION in combination with medications that suppress the release of calcium from the bones or the diuretic medication furosemide (Lasix), which blocks the KIDNEYS from reabsorbing calcium from the blood. When the cause is hyperparathyroidism, the most viable treatment option may be surgery to remove the parathyroid glands. When hypercalcemia results from benign causes, treatment usually resolves the situation and blood calcium levels return to normal.

See also CALCITONIN; MULTIPLE ENDOCRINE NEOPLASIA (MEN); NEPHROLITHIASIS; PHEOCHROMOCYTOMA.

hyperkalemia A circumstance of elevated potassium in the BLOOD circulation. The most common

cause of hyperkalemia is kidney dysfunction in which the KIDNEYS retain excessive potassium in the blood. Such dysfunction may develop as a consequence of RENAL FAILURE or due to endocrine disorders such as ADRENAL INSUFFICIENCY. Hyperkalemia may develop in people who have poorly controlled DIABETES as a consequence of chronically elevated blood GLUCOSE levels, which damages kidney function. Sometimes potassium-sparing diuretic medications, which doctors may prescribe to treat HEART FAILURE or HYPERTENSION (high BLOOD PRESSURE), can result in hyperkalemia. Moderate to severe hyperkalemia causes ARRHYTHMIA (disturbance of the heartbeat).

Weakness and tiredness are the most common symptoms. The diagnostic path includes blood tests to measure the level of potassium and other electrolytes in the blood and ELECTROCARDIOGRAM (ECG) to evaluate the HEART's electrical activity. Treatment consists of appropriate methods to reduce potassium levels according to the underlying cause. Such methods may include changing medications or doses for diuretics, HORMONE THERAPY to supplement adrenal function, reducing consumption of foods high in potassium (such as bananas, green leafy vegetables, and raisins), or therapies to improve kidney function. Most people who have uncomplicated hyperkalemia fully recover with appropriate treatment.

See also ADRENAL GLANDS; ALDOSTERONE; HYPERALDOSTERONISM.

hypernatremia A circumstance of elevated sodium in the BLOOD circulation. The most common cause of hypernatremia is DEHYDRATION that results from prolonged NAUSEA and VOMITING. Rarely, hypernatremia results from DIABETES INSIPIDUS or other dysfunctions of ANTIDIURETIC HORMONE (ADH) release from the HYPOTHALAMUS or PITUITARY GLAND that causes the KIDNEYS to increase the amount of water they pass from the body. The concentration of sodium in the blood correspondingly rises.

The primary symptom of hypernatremia is extreme thirst. As the concentration of sodium increases symptoms become neurologic and include confusion and seizures. The diagnostic path starts with blood tests to measure sodium and other electrolyte levels in the blood and may include a water-deprivation test, which measures the body's endocrine responses (such as increased ADH release) to the shift in electrolyte concentrations. Treatment is increased fluid to restore the appropriate water–sodium balance in the blood. When the cause is diabetes insipidus or other ADH-related insufficiency (such as pituitary dysfunction), treatment typically incorporates HORMONE THERAPY with ADH supplement.

See also ADENOMA; HYPERCALCEMIA; HYPOKALEMIA.

hyperparathyroidism A condition in which the PARATHYROID GLANDS secrete an excessive amount of PARATHYROID HORMONE. The four tiny parathyroid glands are on the back of the THYROID GLAND. Parathyroid hormone regulates the balance of calcium and phosphorus in the BLOOD. Excessive parathyroid hormone results in too much calcium pulled from the bones and absorbed from the gastrointestinal tract into the BLOOD circulation (HYPERCALCEMIA). At the same time blood levels of phosphorus drop (hypophosphatemia). Phosphorus helps retain calcium in the bones and is important for BONE STRENGTH. Calcium is also essential for the conduction of NERVE impulses and for MUSCLE contraction. Excessive calcium in the blood disrupts neuromuscular functions.

The most common cause of hyperparathyroidism is an ADENOMA (noncancerous tumor) of a parathyroid gland. Sometimes the parathyroid glands enlarge (parathyroid HYPERPLASIA) without apparent cause. Either circumstance results in increased secretion of parathyroid hormone. Symptoms of hyperparathyroidism tend to be nonspecific and include

- weakness and rapid tiring with physical exertion
- loss of APPETITE
- lethargy and fatigue
- generalized aches and discomforts

OSTEOPOROSIS may be the first indication of hyperparathyroidism in many people. Sometimes conditions such as HYPERTENSION (high BLOOD PRESSURE), a consequence of calcium's actions, or kidney stones (NEPHROLITHIASIS) reveal the underlying cause to be hyperparathyroidism. The diagnostic path includes blood tests to measure the levels of

calcium, phosphorus, and parathyroid hormone in the blood circulation. Further diagnostic procedures to determine the cause of the hyperparathyroidism may include ULTRASOUND of the neck to evaluate the parathyroid glands, as well as tests of kidney function and X-rays to evaluate bone structure and density. Treatment for parathyroid adenoma or parathyroid hyperplasia typically involves surgery to remove the affected parathyroid gland, which permanently ends the oversecretion. Most people recover fully and without residual consequences unless osteoporosis has become significant and requires subsequent treatment.

See also CALCITONIN; HYPOPARATHYROIDISM; PAGET'S DISEASE OF THE BONE; SURGERY BENEFIT AND RISK ASSESSMENT.

hyperprolactinemia A circumstance of elevated PROLACTIN in the BLOOD circulation that occurs when the anterior lobe of the PITUITARY GLAND secretes excessive prolactin. One of the most common causes of hyperprolactinemia is HYPOTHYROIDISM (underactive THYROID GLAND). Hypothyroidism causes the HYPOTHALAMUS to increase THYROTROPIN-RELEASING HORMONE (TRH) secretion in an attempt to increase the thyroid gland's production of thyroid hormones. TRH also stimulates the pituitary gland to release prolactin. Hyperprolactinemia may also result from a prolactin-secreting ADENOMA of the pituitary gland, a noncancerous tumor also called a prolactinoma. Numerous medications may interfere with the endocrine cascades by suppressing DOPAMINE, a HORMONE that "turns off" prolactin secretion.

Hyperprolactinemia has both direct action and cascading effects on the endocrine function. The direct action of prolactin activates the milk ducts in the breasts, causing milk production and lactation. The cascading effects begin with the hypothalamus and carry through the endocrine cascade to the gonads (sex glands) Elevated levels of prolactin in the blood circulation shut off the hypothalamus's production of GONADOTROPIN-RELEASING HORMONE (GNRH), which consequently slows the pituitary gland's production of LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH). These events further lead to reduced production of ESTROGENS, PROGESTERONE, and TESTOSTERONE by the OVARIES, TESTICLES, and ADRENAL GLANDS.

In women the primary symptoms of hyperprolactinemia include disturbances of MENSTRUATION (notably infrequent or absent menstrual periods), INFERTILITY, and milk production (galactorrhea) when not pregnant or BREASTFEEDING. In men the primary symptoms of hyperprolactinemia include ERECTILE DYSFUNCTION and HYPOGONADISM resulting from diminished testosterone levels. When the cause of the hyperprolactinemia is a prolactinoma, both men and women may experience headaches and disturbances of vision from pressure the tumor applies on adjacent structures, such as the OPTIC NERVE, in the BRAIN.

The diagnostic path begins with blood tests to measure the levels of key hormones such as the thyroid hormones, the sex hormones, and prolactin. The results of these tests determine the further course of diagnostic procedures, which may include MAGNETIC RESONANCE IMAGING (MRI) of the head to evaluate the possibility of prolactinoma or ULTRASOUND of the neck to assess the thyroid gland. Treatment targets the underlying cause of the excessive prolactin secretion, which may require surgery to remove an adenoma or medications (dopamine agonists, which suppress prolactin secretion) to treat prolactinoma, or hormone replacement therapy to treat hypothyroidism. Most people recover fully and without residual consequences after appropriate treatment, though may require ongoing treatment for the identified underlying conditions.

See also HYPOPITUITARISM; OSTEOPOROSIS; SURGERY BENEFIT AND RISK ASSESSMENT.

hyperthyroidism A condition, also called thyrotoxicosis, in which the THYROID GLAND overproduces thyroid hormones. The excessive thyroid hormones accelerate METABOLISM.

In health the endocrine system maintains a precise balance among the thyroid hormones to regulate many of the functions of metabolism. The thyroid hormonal cascade begins when the HYPOTHALAMUS produces THYROTROPIN-RELEASING HORMONE (TRH). TRH stimulates the anterior lobe of the PITUITARY GLAND to release THYROID-STIMULATING HORMONE (TSH). TSH stimulates the thyroid gland to synthesize TRIIODOTHYRONINE (T_3) and THYROXINE (T_4), the major active thyroid hormones, as well as several minor or precursor (inactive) thyroid hormones.

When T_3 and T_4 reach appropriate levels in the BLOOD circulation, the hypothalamus ceases TRH production and the thyroid hormone cascade tapers off.

Hyperthyroidism may result from a dysfunction of the thyroid hormone cascade (usually a failure of the pituitary gland to appropriately produce TSH) or overactivity of the thyroid gland. Pituitary ADENOMA is the most common cause of TSH-based hyperthyroidism. Pituitary adenomas secrete TSH that is more potent than normal TSH, eliciting a stronger response from the thyroid gland. Hyperthyroidism that arises from overactivity of the thyroid gland may have various causes. Among them are

- GRAVES'S DISEASE, an autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack thyroid tissue
- damage to the thyroid gland resulting from radiation exposure (including RADIATION THERAPY involving structures of the neck, lower face, or upper chest)
- thyroid nodules (nearly always noncancerous)
- excessive consumption of iodine, often resulting from medications that contain iodine (such as the antiarrhythmia medication amiodarone)
- THYROIDITIS (INFLAMMATION of the thyroid gland)
- excessive consumption of therapeutic thyroid hormone supplements (also called thyrotoxicosis factitia)
- THYROID CANCER, which is rare

A dangerous weight loss practice is the intentional consumption of thyroid HORMONE supplement by people who have normal thyroid function. Though this accelerates METABOLISM to generate weight loss, the resulting state of hyperthyroidism can cause serious disturbances of the HEART'S rhythm (ARRHYTHMIA) and the life-threatening condition THYROID STORM, which requires emergency medical treatment. Only people with diagnosed HYPOTHYROIDISM (underactive thyroid) should take thyroid hormone supplement, and only at the DOSE the doctor prescribes.

Symptoms and Diagnostic Path

Hyperthyroidism tends to develop over weeks to months with few indications until thyroid HORMONE levels become significantly elevated, such that the condition may be quite advanced by the time the person becomes aware of symptoms. The most common symptoms of hyperthyroidism are

- racing PULSE and PALPITATIONS
- weight loss
- feeling hot and intolerance to environmental heat
- moist, warm SKIN
- irritability, anxiety, and insomnia (difficulty sleeping)

GOITER (enlarged thyroid gland) is common. People who have Graves's disease may also have EXOPHTHALMOS (bulging eyes, also called poptosis) and autoimmune symptoms involving the SKIN and other body systems. The diagnostic path begins with blood tests to measure the levels of the thyroid hormones in the blood circulation. In hyperthyroidism that originates with the thyroid gland, T_3 and T_4 are usually elevated and TSH is lower than normal. When there is a dysfunction of TSH or the thyroid hormone cascade, T_3 and T_4 are elevated and TSH is normal. Further diagnostic procedures to determine the cause of the hyperthyroidism may include ULTRASOUND or radioiodine scan (also called radioactive-reuptake scan) of the neck to detect nodules or inflammation of the thyroid gland.

Treatment Options and Outlook

Treatment targets reducing thyroid hormone production. Such an approach may include antithyroid medications, radioactive iodine, or surgery to remove part or all of the thyroid gland. The appropriate treatment depends on the circumstances of the hyperthyroidism and the person's overall health status. Antithyroid medications, commonly methimazole and propylthiouracil (PTU), work by interfering with thyroid hormone synthesis and with conversion of T_4 to T_3. Antithyroid medication therapy must be continuous; most people experience a return of hyperthyroidism when they stop taking the medications.

Radioactive iodine, ^{131}I, which destroys thyroid tissue, and surgery to remove part or all of the

thyroid gland provide permanent solutions to thyroid hormone overproduction. Most people subsequently require long-term thyroid hormone supplements (HORMONE THERAPY) to maintain adequate thyroid hormone levels in the blood, as these treatments often leave the thyroid gland incapable of synthesizing thyroid hormones. Total thyroidectomy always requires thyroid hormone replacement.

When the hyperthyroidism is likely transitory, as with thyroiditis, treatment may target only symptom relief because thyroid function will return to normal when the inflammation subsides. Beta blocker medications (notably propanolol) relieve the symptoms that are the most distressing—palpitations, irritability, and heat insensitivity. Endocrinologists also sometimes prescribe beta blockers in conjunction with antithyroid therapies when these symptoms cause pronounced discomfort, until thyroid function returns to normal.

A life-threatening complication of untreated hyperthyroidism is THYROID STORM, in which there are extensive cardiovascular and NERVOUS SYSTEM responses to the elevated thyroid hormone levels. Often, thyroid storm manifests in a person who is unaware of having hyperthyroidism who develops another health condition that stresses the body. Congestive HEART FAILURE, serious arrhythmias, and cardiovascular SHOCK can develop very rapidly and require emergency medical treatment.

Risk Factors and Preventive Measures

Exposure to radiation and excessive iodine consumption are the primary known risk factors for hyperthyroidism. People who have other AUTOIMMUNE DISORDERS are more likely to develop Graves's disease. The only preventable forms of hyperthyroidism are those which result from overconsumption of thyroid-hormone supplements and medication therapies that result in excessive iodine consumption. Otherwise, there are no known measures for preventing hyperthyroidism.

See also GRAVES'S OPHTHALMOPATHY; HYPOTHYROIDISM.

hypoadrenocorticism See ADDISON'S DISEASE.

hypocalcemia A circumstance of insufficient calcium in the BLOOD circulation. Common causes of hypocalcemia include chronic DIARRHEA, which prevents calcium absorption from dietary sources, and lack of sun exposure, which prevents activation of vitamin D (crucial for calcium absorption). HYPOPARATHYROIDISM is the most common endocrine cause for hypocalcemia, and may result from atrophy, dysfunction, or surgical removal of the PARATHYROID GLANDS. Some people develop resistance to PARATHYROID HORMONE, usually as a consequence of vitamin D deficiency.

Calcium is essential for many functions within the body, notably the conduction of NERVE impulses and MUSCLE contractions. Inadequate calcium in the blood disrupts these functions and may result in ARRHYTHMIA (irregular HEART RATE), HYPOTENSION (low BLOOD PRESSURE), mental confusion and irritability, and muscle spasms (tetany). Severely low levels of calcium in the blood can cause seizures, and prolonged hypocalcemia can result in PAPILLEDEMA (swelling where the OPTIC NERVE exits the RETINA) and permanent damage to the CORNEA.

The diagnostic path includes blood tests to measure the levels of calcium and parathyroid hormone in the blood, a comprehensive NEUROLOGIC EXAMINATION, and an ELECTROCARDIOGRAM (ECG) to assess any irregularities in the functioning of the HEART. Other diagnostic procedures may include X-rays of the bones, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) scan, or MAGNETIC RESONANCE IMAGING (MRI) to visualize the parathyroid glands. Treatment targets any underlying conditions, then focuses on restoring appropriate calcium balance in the body, typically through dietary changes to increase the amount of calcium in the diet, and with calcium and vitamin D supplements. Most people recover fully and without residual consequences with appropriate treatment. Long-term treatment may be necessary, depending on the cause of the hypocalcemia.

See also CHEMOTHERAPY; FANCONI'S SYNDROME; PANCREATITIS; POLYGLANDULAR DEFICIENCY SYNDROME; SEIZURE DISORDERS.

hypoglycemia A circumstance in which the BLOOD GLUCOSE level is too low. A normal blood glucose level is 70 milligrams per deciliter (ml/dL) to 100 mg/dL. The clinical standard for hypoglycemia is a blood glucose level below 50 mg/dL,

though some people may experience symptoms of hypoglycemia with blood glucose levels between 50 mg/dL and 70 mg/dL.

Hypoglycemia most commonly occurs in people who have DIABETES, manifesting as a consequence of taking more INSULIN or antidiabetes medication than is necessary to balance carbohydrate consumption or due to a more intense level of physical activity than usual, which increases the body's need for glucose. Hypoglycemia also can occur in people who do not have diabetes, often as a result of inadequate carbohydrate consumption particularly during intense physical exercise or with extended fasting (going without food). Excessive ALCOHOL consumption, particularly in people who have CIRRHOSIS of ALCOHOLISM or other LIVER disease, may also cause hypoglycemia. An uncommon form of nondiabetes hypoglycemia is reactive hypoglycemia, in which the blood glucose level drops within three to four hours after eating. Researchers do not know what causes reactive hypoglycemia.

Imbalances or dysfunctions of the endocrine system's hormonal cascades may slow the body's efforts to restore adequate blood glucose levels. In health, a low blood glucose level triggers the ISLETS OF LANGERHANS to release GLUCAGON, which directs the liver to convert glycogen (a storage form of glucose) to glucose. Simultaneously, the HYPOTHALAMUS releases CORTICOTROPIN-RELEASING HORMONE (CRH) and GROWTH HORMONE–RELEASING HORMONE (GHRH), which set in motion hormonal cascades to alter METABOLISM in ways that slow the body's use of glucose.

The symptoms of hypoglycemia include

- feeling weak and shaky
- hunger
- excessive sweating
- drowsiness and confusion
- acting intoxicated
- dizziness and lightheadedness

People who have diabetes should check their blood glucose levels at the onset of any of these symptoms. Immediate treatment generally resolves the symptoms, and may include drinking a glass of juice or soda (regular, not diet or sugar-free products), eating a spoonful of sugar or honey, or eating a small amount of candy. The doctor may follow up with diagnostic tests to determine the cause of the hypoglycemic episode, such as blood tests to measure glucose levels during symptoms. The body's needs for insulin and glucose vary with physical activity, so people who have diabetes may need to adjust their medication doses if they increase their exercise levels and experience repeated episodes of hypoglycemia. Eating small meals frequently (every three hours) maintains a more consistent level of glucose in the blood circulation and is the therapeutic approach doctors recommend for people who have reactive hypoglycemia. Though untreated hypoglycemia can have significant consequences including coma and death, most people respond quickly to treatment and recover without residual effects.

See also INSULIN RESISTANCE.

hypokalemia A circumstance of low potassium in the BLOOD circulation. There are many causes of hypokalemia. Among the most common are persistent DIARRHEA (which depletes electrolytes from the body), long-term therapy with diuretic medications (many of which cause the KIDNEYS to excrete potassium), and kidney disease (which affects the ability of the kidneys to regulate potassium retention). Endocrine causes for hypokalemia include HYPERALDOSTERONISM (oversecretion of ALDOSTERONE) and excessive ADRENOCORTICOTROPIN HORMONE (ACTH) such as occurs with CUSHING'S SYNDROME.

The symptoms of hypokalemia are those of electrolyte imbalance. Mild to moderate symptoms may include MUSCLE weakness or cramping, fatigue, and excessive thirst. Significant hypokalemia can cause confusion, disorientation, and ARRHYTHMIA (irregular heartbeat). Without treatment hypokalemia has the potential to be fatal as it can result in HEART ATTACK or PARALYSIS of the muscles that impairs BREATHING.

The diagnostic path begins with blood tests that measure the levels of potassium, sodium, magnesium, and other electrolytes in the blood. An ELECTROCARDIOGRAM (ECG) identifies any arrhythmias. Treatment is potassium supplementation, which may need to be intravenous when symptoms are severe. Potassium tablets (as the doctor prescribes)

or foods high in potassium such as bananas, oranges, potatoes, and green leafy vegetables can provide adequate potassium supplementation for mild to moderate hypokalemia.

See also FANCONI'S SYNDROME; HYPERKALEMIA; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; RENAL FAILURE.

hyponatremia A circumstance of insufficient sodium in the BLOOD circulation. Hyponatremia is a symptom of numerous underlying health conditions rather than itself a disorder. The most common cause of hyponatremia is DEHYDRATION, typically as a consequence of extended VOMITING and DIARRHEA or of diuretic therapy (medications taken to reduce the volume of fluid in the body, many of which work by causing the KIDNEYS to increase the amount of sodium they pass from the body in the URINE). Among the endocrine conditions that cause hyponatremia are HYPOTHYROIDISM, ADRENAL INSUFFICIENCY, ADDISON'S DISEASE, and hypoaldosteronism. Nonendocrine systemic disorders that can cause hyponatremia include NEPHROTIC SYNDROME, RENAL FAILURE, CIRRHOSIS, LIVER FAILURE, and congestive HEART FAILURE.

Mild hyponatremia may show no symptoms, with the doctor making the detection during blood tests done for various reasons to measure electrolyte levels. Moderate to severe hyponatremia has primarily neurologic symptoms, as the imbalance between sodium and water in the BRAIN affects communication among neurons (NERVE cells). Symptoms include confusion, cognitive dysfunction, and changes in mood or personality. The diagnostic path typically includes blood tests to measure the amounts of sodium and other electrolytes in the blood, urinalysis to measure the proportions of excreted electrolytes to water, and appropriate tests and procedures to evaluate any suspected endocrine or other health conditions that could be responsible for the hyponatremia.

Hyponatremia requires prompt medical treatment to restore the sodium balance in the blood circulation. Often, identifying and targeting the underlying cause (such as reducing the DOSE of a diuretic medication or hormone supplementation therapy to restore hormonal balance) brings about homeostasis. Untreated hyponatremia can lead to cerebral edema (swelling in the brain), loss of consciousness, and death. When the cause is endocrine dysfunction, such as hypothyroidism or Addison's disease, lifelong HORMONE THERAPY is typically necessary. Many people fully recover from hyponatremia though may need ongoing medical treatment for the underlying health condition.

See also ALCOHOLISM; COGNITIVE FUNCTION AND DYSFUNCTION; HYPERNATREMIA; MALNUTRITION; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE.

hypoparathyroidism A rare condition in which the amount of PARATHYROID HORMONE in the BLOOD circulation is insufficient, as a consequence of either dysfunction or absence of the PARATHYROID GLANDS. Thyroidectomy (surgical removal of the THYROID GLAND, such as to treat THYROID CANCER) is the most common reason for absence of the parathyroid glands, as the four parathyroid glands rest on the back surface of the thyroid gland. Occasionally the parathyroid glands are the target of an autoimmune attack that destroys their ability to function. Rarely, the parathyroid glands are absent from birth, a congenital anomaly that requires lifelong calcium and vitamin D supplement therapy to maintain adequate blood calcium levels as well as BONE STRENGTH and density.

Hypoparathyroidism results in inadequate calcium (HYPOCALCEMIA) and excessive phosphorus (hyperphosphatemia) in the blood. The symptoms of hypoparathyroidism are those of hypocalcemia and may include

- tingling of the toes, fingers, and lips
- MUSCLE cramps
- rarely, seizures

The diagnostic path includes blood tests to measure the levels of calcium, phosphate, and parathyroid hormone in the blood circulation. Treatment for confirmed hypoparathyroidism is supplementation with calcium and vitamin D. When the parathyroid glands are missing or destroyed, lifelong treatment is necessary.

See also HYPERCALCEMIA; HYPERPARATHYROIDISM; MINERALS AND HEALTH; OSTEOPOROSIS; VITAMINS AND HEALTH.

hypopituitarism A condition in which the PITUITARY GLAND secretes an insufficient amount of one

or more of the hormones it produces. There are numerous causes for hypopituitarism, some of which are transient and others that require lifelong HORMONE THERAPY to supplement hormone deficiencies. Tumors, INFECTION, trauma, and AUTOIMMUNE DISORDERS are the most common causes of pituitary damage resulting in hypopituitarism. AMYLOIDOSIS and SARCOIDOSIS may also cause hypopituitarism. Occasionally the deficiencies result from damage to the HYPOTHALAMUS, which regulates pituitary function, or to the communication between the hypothalamus and the pituitary gland. Deficiencies may involve any of the hormones the anterior lobe of the pituitary gland synthesizes.

The diagnostic path includes BLOOD tests to measure HORMONE levels. The endocrinologist may choose to conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) to evaluate the structural integrity of the involved endocrine glands. Treatment consists of appropriate hormone therapy, usually lifelong, to supplement deficient hormones.

See also HYPERPROLACTINEMIA; POLYGLANDULAR DEFICIENCY SYNDROME.

hypothalamus A structure of the midbrain that has both neurologic and endocrine functions, serving as a bridge between the neurologic system and the endocrine system. A construction of primarily NERVE cells, the hypothalamus receives and processes myriad signals from the BRAIN and central NERVOUS SYSTEM about vital functions such as BREATHING, HEART RATE, BLOOD PRESSURE, body temperature (thermoregulation), and fluid balance. In response to these neurologic signals specific centers in the hypothalamus synthesize (produce) numerous hormones that direct the PITUITARY GLAND to secrete or stop secreting the hormones it synthesizes or stores.

A dedicated network of BLOOD vessels connects the hypothalamus and the pituitary gland, which lies beneath the hypothalamus, allowing hypothalamic hormones to travel through the blood directly to the pituitary gland and fostering intimate and continuous communication between the two structures. In turn, the hormones the pituitary gland produces enter the general circulation to direct the functions of other endocrine glands. Through this cascading hormonal regulation the hypothalamus controls, in integration with neurologic processes, most core functions essential for survival.

Hypothalamic Hormones

The hormones the hypothalamus produces are peptides (amino acid structures) that target specific cell clusters within the pituitary gland's two lobes, acting either to stimulate or inhibit pituitary gland activity. The hypothalamic hormones are

PITUITARY HORMONE DEFICIENCIES

Deficient Hormone	Consequences
deficient ADRENOCORTICOTROPIN HORMONE (ACTH)	ADRENAL INSUFFICIENCY: HYPOTENSION, HYPOGLYCEMIA, fatigue
deficient GROWTH HORMONE (GH)	children: stunted growth adults: slowed METABOLISM
deficient LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH)	women: cessation of OVULATION and MENSTRUAL CYCLES, INFERTILITY, masculinization men: HYPOGONADISM, infertility, ERECTILE DYSFUNCTION, feminization
deficient THYROID-STIMULATING HORMONE (TSH)	HYPOTHYROIDISM: weight gain, confusion, intolerance to cold, chronic CONSTIPATION
deficient PROLACTIN	BREASTFEEDING women: inability to produce milk

- ANTIDIURETIC HORMONE (ADH), which the pituitary gland stores and releases to regulate the amount of water the KIDNEYS retain in the blood as one of the body's mechanisms for controlling blood pressure
- CORTICOTROPIN-RELEASING HORMONE (CRH), which stimulates the pituitary gland to release ADRENOCORTICOTROPIN HORMONE (ACTH) as the first level in the body's STRESS RESPONSE HORMONAL CASCADE
- DOPAMINE, which inhibits pituitary gland production of FOLLICLE-STIMULATING HORMONE (FSH), LEUTEINIZING HORMONE (LH), THYROID-STIMULATING HORMONE (TSH), and PROLACTIN
- GONADOTROPIN-RELEASING HORMONE (GNRH), which stimulates the pituitary gland to synthesize and release LH and FSH, hormones that are fundamental to reproduction
- GROWTH HORMONE–RELEASING HORMONE (GHRH), which stimulates the pituitary gland to synthesize and release GROWTH HORMONE (GH)
- OXYTOCIN, which the pituitary gland subsequently stores and releases when needed to stimulate contractions of the UTERUS during CHILDBIRTH and to influence sexual arousal in both men and women
- THYROTROPIN-RELEASING HORMONE (TRH), which stimulates the pituitary gland to synthesize and release TSH, initiating hormonal regulation of vital functions such as thermal regulation and cellular METABOLISM, and to produce prolactin, which stimulates milk production during BREASTFEEDING

Structure of the Hypothalamus

Despite the vital and extensive nature of its functions, the hypothalamus is physically a small structure not quite the size and shape of an almond. Within the hypothalamus are a number of functionally distinct substructures, called nuclei, each having unique and specific roles that require intimate integration with one another. The major nuclei that have endocrine functions are the

- supraoptic nucleus, which synthesizes and releases ADH
- paraventricular nucleus, which synthesizes and releases oxytocin, CRH, and TRH
- arcuate nucleus, which synthesizes and releases GHRH
- suprachiasmatic nucleus (SCN), which influences the circadian cycle and various body rhythms through the cyclic release of certain hormones
- ventromedial nucleus, which regulates APPETITE

Disorders and dysfunctions of the hypothalamus are extremely rare, and when they do occur tumors are the most likely cause. Disorders and dysfunctions of other endocrine glands can affect the ways those glands respond to hypothalamic hormones. Long-term, chronic ALCOHOL abuse destroys hypothalamic cells, affecting the endocrine and neurologic functions of the hypothalamus.

HYPOTHALAMIC HORMONES

ANTIDIURETIC HORMONE (ADH)	CORTICOTROPIN-RELEASING HORMONE (CRH)
DOPAMINE	GROWTH HORMONE–RELEASING HORMONE (GHRH)
GONADOTROPIN-RELEASING HORMONE (GNRH)	SOMATOSTATIN
OXYTOCIN	
THYROTROPIN-RELEASING HORMONE (TRH)	

For further discussion of the hypothalamus within the context of the endocrine system's structure and function please see the overview section "The Endocrine System." For further discussion of the hypothalamus within the context of neurologic structures and functions please see the overview section "The Neurologic System."

See also ADRENAL GLANDS; OBESITY; PINEAL GLAND; THYMUS; THYROID GLAND.

hypothyroidism A condition in which the THYROID GLAND secretes an insufficient amount of thyroid hormones. It is the most common disorder of thyroid function, affecting about 7 million Americans. Women are eight times more likely than men to have hypothyroidism. Risk for hypothyroidism increases among men and women with advancing age. Health experts estimate 80 percent of people over age 70 have hypothyroidism, though the rate of diagnosis is not this high.

The thyroid hormones, primarily THYROXINE (T_4) and TRIIODOTHYRONINE (T_3), regulate METABOLISM in every cell. Deficiencies of these hormones cause numerous symptoms that reflect slowed metabolism. The consequences can be particularly significant when hypothyroidism occurs in children, interfering with physical growth and intellectual development. Congenital hypothyroidism (formerly called cretinism) can cause permanent impairments. Fortunately congenital hypothyroidism is rare in the United States because newborn and well-child health-care screenings test for hypothyroidism.

The follicular cells of the thyroid gland synthesize (manufactures) thyroid hormones from the amino acid tyrosine and the mineral iodine, both of which it acquires from dietary sources. A shortage of either in the diet, though very uncommon in the United States, can impair thyroid HORMONE synthesis. The hypothalamus initiates the hormonal cascade that results in thyroid hormone production, secreting THYROID-RELEASING HORMONE (TRH) when T_3 and T_4 levels in the BLOOD circulation drop. TRH stimulates the anterior lobe of the PITUITARY GLAND to produce THYROID-STIMULATING HORMONE (TSH), which in turn stimulates the thyroid gland's follicular cells. Rising T_3 and T_4 levels in the blood then reverse the hormonal cascade.

Sometimes the cause of hypothyroidism is clear. Hypothyroidism is certain in anyone who has had a total thyroidectomy (removal of the thyroid gland, such as to treat THYROID CANCER or GRAVES'S DISEASE) and likely in a person who has had a partial thyroidectomy. Treatment for HYPERTHYROIDISM (overactive thyroid gland) often results in eventual hypothyroidism as follicular cells within the thyroid gland continue to die after treatment ends. The most common identifiable cause is THYROIDITIS, an INFLAMMATION of the thyroid gland that destroys follicular cells and that may be an autoimmune process. Most often, however, hypothyroidism is idiopathic—the cause remains unknown.

Symptoms and Diagnostic Path

The symptoms of hypothyroid appear gradually and are often nonspecific. They typically include

- chronic tiredness
- weight gain or inability to lose weight
- DEPRESSION and irritability
- coarsening HAIR and hair loss
- dry, flaky SKIN
- loss of eyebrow hair
- intolerance to cold or feeling cold regardless of the environmental temperature
- irregular MENSTRUATION and INFERTILITY

Some people also have a GOITER, a painless swelling of the thyroid gland that may be visible when looking in the mirror or that the doctor can feel. The diagnostic path begins with blood tests to measure the levels of thyroid hormones in the blood circulation. A low level of T_3 and T_4 coupled with elevated TSH indicates the thyroid gland is not responding to the pituitary gland's hormonal signals and provides a conclusive diagnosis of hypothyroidism. Some people have borderline blood test results though have hypothyroidism nonetheless. When blood thyroid levels are marginal, the doctor may recommend a trial of treatment to see if symptoms improve.

Treatment Options and Outlook

Treatment is HORMONE THERAPY with thyroid hormone supplement to deliver adequate levels of thyroid hormones. The most common form of thyroid hormone supplement is a synthetic pharmaceutical preparation of T_4 (levothyroxine). This provides adequate thyroid hormones for most people because the cells in the body convert T_4 to T_3 when it binds with them. There are several levothyroxine products available. Endocrinologists recommend staying with the same product consistently, as the formulations of each product are somewhat different. Some doctors also prescribe T_3 hormone supplement, which is faster-acting, in combination with a T_4 hormone supplement, as an approach that attempts to more precisely replicate the body's thyroid hormone synthesis. The doctor also may prescribe a short course of T_3 to rapidly bring thyroid hormone levels up when hypothyroidism is severe, then taper off and resume T_4 supplement.

Most people experience some improvement of symptoms within two weeks of starting hormone therapy. However, it may take six months to a

year to establish the most effective DOSE, during which time the doctor will routinely measure the thyroid hormones in the blood and compare them with changes in symptoms and the overall clinical picture. Most people experience a vast improvement within a month of beginning hormone therapy. Treatment is lifelong. Undertreated or untreated hypothyroidism results in progressively worsening symptoms that can culminate in permanent damage to the cardiovascular and neurologic systems. People over age 60 typically need lower doses of thyroid hormone supplement for therapeutic results.

Risk Factors and Preventive Measures

The key risk factors for hypothyroidism are being female and age over 60; being both female and over 60 in combination increases the risk because of estrogen's role in hormone balance. People who have received RADIATION THERAPY to the lower face, neck, or upper chest have increased risk for hypothyroidism. Lithium, a medication taken for BIPOLAR DISORDER, may disrupt thyroid function and cause hypothyroidism. There are no measures to prevent hypothyroidism.

See also AUTOIMMUNE DISORDERS; CALCITONIN; ESTROGENS; EUTHYROID SICK SYNDROME.

I

inhibin A peptide HORMONE the corpus luteum in ovulating women and the TESTES in men produce that stops the HYPOTHALAMUS from secreting GONADOTROPIN-RELEASING HORMONE (GNRH). This in turn stops the PITUITARY GLAND from secreting LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH), halting the subsequent cascade of sex hormones from the gonads (sex glands). Researchers do not yet fully understand the full range of inhibin's actions, though it influences spermatogenesis (SPERM production) in men and likely has additional roles in OVULATION. Some research suggests inhibin may serve as a marker to indicate an emerging OVARIAN CANCER or PROSTATE CANCER. With the cessation of ovulation a woman's OVARIES no longer produces inhibin, so inhibin is no longer present in the BLOOD circulation of postmenopausal women. Inhibin production returns, however, when there is an ovarian cancer. Conversely, inhibin levels appear to drop in men who have BENIGN PROSTATIC HYPERTROPHY (BPH) or prostate cancer.

For further discussion of inhibin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also FERTILITY; PREGNANCY; TESTOSTERONE.

insulin A peptide HORMONE the ISLETS OF LANGERHANS in the PANCREAS produce that is essential for the body to use GLUCOSE. Insulin has numerous roles in the body, the best known of which is the regulation of glucose levels in the BLOOD (carbohydrate METABOLISM). Glucose, a basic sugar molecule, is a primary energy source for many cellular activities. When insulin binds with insulin receptors on a cell membrane, the cell allows glucose molecules to enter. Insulin facilitates lipid (fatty acid) metabolism, stimulates the LIVER to convert excess glucose into the intermediary storage form glycogen, and facilitates the conversion of amino acids to proteins for building new MUSCLE tissue. Insulin also participates in cell activities related to growth.

The beta cells of the islets of Langerhans synthesize insulin in response to declining glucose levels in the blood. The release of insulin allows cells to accept glucose and at the same time directs the liver to begin converting glucose to glycogen for storage. Insulin also slows the conversion of fatty acids to glycogen, a process intended to conserve the long-term energy resources of the body (fat). These functions become less efficient in INSULIN RESISTANCE, a condition in which the cells are slow to bind with insulin. Disturbances of insulin sensitivity can allow lipids to accumulate in the blood circulation, contributing to cardiovascular diseases such as ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). Insufficient insulin production results in DIABETES, for which insulin is available as an injectable pharmaceutical as HORMONE THERAPY. Most forms of insulin available today are recombinant constructions engineered in the laboratory to precisely match the molecular structure and actions of endogenous human insulin.

For further discussion of insulin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also CORTISOL; DIGESTIVE ENZYMES; DIGESTIVE HORMONES.

insulin resistance A condition, also called metabolic syndrome X or syndrome X, in which the cells

throughout the body do not respond to the normal amounts of INSULIN the ISLETS OF LANGERHANS produce. The short-term result is an excessive level of GLUCOSE in the BLOOD circulation and the need for the islet cells to produce increasing amounts of insulin. Over the long term a constellation of health conditions appears that may include OBESITY, HYPERLIPIDEMIA, type 2 DIABETES, CORONARY ARTERY DISEASE (CAD), HYPERTENSION (high BLOOD PRESSURE), and POLYCYSTIC OVARY SYNDROME (PCOS). Doctors diagnose insulin resistance when a person has two or more of these health conditions.

Treatment must first target the health condition, and may include medications to reduce blood pressure and blood cholesterol levels. CAD may have significant implications for cardiovascular function, and is a major risk for HEART ATTACK as well as HEART FAILURE, CARDIOMYOPATHY, and ISCHEMIC HEART DISEASE (IHD). Weight loss is crucial as OBESITY is a key factor in these conditions as well as in insulin resistance. Lifestyle measures such as nutritious EATING HABITS and daily physical exercise help improve metabolic efficiency and sensitivity to insulin and also aid weight-management efforts. These lifestyle measures practiced consistently over time are often able to reverse some of the health consequences as insulin resistance diminishes, in particular facilitating improvements in obesity, hypertension, and type 2 diabetes.

See also BODY MASS INDEX (BMI); DIABETES AND CARDIOVASCULAR DISEASE; DIET AND HEALTH; EXERCISE AND HEALTH; HEALTH RISK FACTORS; INFERTILITY; LIFESTYLE AND HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

islets of Langerhans Clusters of endocrine cells distributed throughout the PANCREAS that produce INSULIN, GLUCAGON, and SOMATOSTATIN. There are about a million islet clusters, each containing several hundred islet cells. Each islet contains all three types of islet cells: alpha islet cells, beta islet cells, and delta islet cells.

In the center of each islet are the beta cells, which secrete insulin. Insulin's primary role in the body is the regulation of carbohydrate METABOLISM. Arranged in somewhat of a circle around the core of the islet beta cells are the alpha cells, which secrete glucagon, and the delta cells, which secrete somatostatin. Glucagon stimulates the LIVER to convert glycogen to GLUCOSE, making more energy available to cells. Somatostatin suppresses the release of GROWTH HORMONE (GH). It also slows the release of insulin and glucagon, as well as the gastrointestinal system's secretion of DIGESTIVE HORMONES.

The most significant disorder affecting the islets of Langerhans is DIABETES. Type 1 diabetes, an autoimmune disorder, destroys the islet cells. Though other cells in the body synthesize the hormones of alpha and delta islet cells—glucagon and somatostatin, respectively—no other cells in the body synthesize insulin. People who have type 1 diabetes must take insulin therapy (injections of pharmaceutical insulin) to meet the needs of their bodies for this crucial hormone. PANCREATITIS, an INFLAMMATION of the pancreas, also can interfere with islet cell functions. Though HORMONE production usually returns when the inflammation subsides, sometimes extensive scarring destroys islet cells, resulting in type 2 (insulin-deficient) diabetes.

For further discussion of the islets of Langerhans within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also AUTOIMMUNE DISORDERS; DIGESTIVE ENZYMES; POLYGLANDULAR DEFICIENCY SYNDROME.

islet cell transplantation An experimental treatment for DIABETES in which the surgeon injects clusters of healthy ISLET OF LANGERHANS cells from a donor (most often a cadaver donor) into the PANCREAS of a person who has type 1 diabetes. Islet cells produce the HORMONE INSULIN as well as two other hormones, GLUCAGON and SOMATOSTATIN. A healthy pancreas contains about a million clusters of islet cells distributed widely throughout the pancreatic tissue. Type 1 diabetes occurs when an autoimmune response destroys the islet cells, eliminating the body's ability to produce insulin. Islet cell transplantation replaces the destroyed cells with healthy islet cells. It may take weeks to months for the transplanted islet cells to establish networks of BLOOD vessels that connect them to the recipient and provide the outlet for the

hormones they produce. At present islet cell transplantation requires subsequent lifelong IMMUNOSUPPRESSIVE THERAPY to prevent rejection of the transplanted cells. Though still experimental, islet cell transplantation holds considerable promise as a long-term or permanent treatment for type 1 diabetes.

See also ORGAN TRANSPLANTATION.

L–O

luteinizing hormone (LH) A peptide HORMONE the anterior lobe of the PITUITARY GLAND produces that stimulates hormonal activity related to reproduction. In men, LH stimulates the development and function of interstitial cells in the TESTES that synthesize and release TESTOSTERONE, the primary male sex hormone. In menstruating women, a mid–menstrual cycle surge of LH stimulates OVULATION (the maturation and release of an ovum, or egg). In a woman who is pregnant, the PLACENTA also produces LH. The HYPOTHALAMUS's release of GONADOTROPIN-RELEASING HORMONE (GNRH) stimulates the pituitary gland to secrete LH. Rising levels of the sex hormones (ESTROGENS, PROGESTERONE, and TESTOSTERONE) and INHIBIN cause the hypothalamus to stop releasing GnHR, ending the pituitary gland's secretion of LH.

For further discussion of LH within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANABOLIC STEROIDS AND STEROID PRECURSORS; ANTIDIURETIC HORMONE (AH); CHORIONIC GONADOTROPIN; FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); MENSTRUATION; OXYTOCIN; PROLACTIN; RELAXIN; THYROID-STIMULATING HORMONE (TSH).

melatonin A peptide HORMONE that the PINEAL GLAND secretes, the primary function of which is to regulate the body's circadian cycle (pattern of sleep and wake). The pineal gland synthesizes melatonin from the amino acid tryptophan. The OPTIC NERVE appears to convey NERVE messages of outside light and dark from the RETINA to a section of the HYPOTHALAMUS called the suprachiasmatic nucleus (SCN). The SCN sends nerve signals to the pineal gland, which suspends melatonin synthesis. Darkness causes the nerve messages from the optic nerve to stop, which in turn ends the signals from the SCN. When receiving signals from the SCN, the pineal gland stops melatonin production. When the signals from the SCN end, the pineal gland resumes melatonin production. Researchers believe melatonin causes sleepiness by slowing cell METABOLISM. Other endocrine processes, such as the adrenocorticosteroid hormonal cascade that regulates CORTISOL levels, also slow in conjunction with the circadian cycle, though researchers are uncertain about how these processes may be interrelated.

For further discussion of melatonin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also MELATONIN SUPPLEMENT; STRESS RESPONSE HORMONAL CASCADE.

multiple endocrine neoplasia (MEN) An inherited genetic disorder in which numerous tumors form in various endocrine glands. Several GENE mutations are responsible for the errant growth of glandular tissue, which may take the form of tumors or hypertrophy (overgrowth). Oversecretion of the affected gland's hormones then occurs. The three forms of MEN are

- MEN-1, in which adenomas develop in the PITUITARY GLAND, PARATHYROID GLANDS, and ISLETS OF LANGERHANS in the PANCREAS
- MEN-2a, characterized by HYPERPARATHYROIDISM, PHEOCHROMOCYTOMA, and medullary THYROID CANCER

- MEN-2b, characterized by pheochromocytoma, neuromas in the mucous membranes of the MOUTH and eyes, and medullary thyroid cancer

The gene MUTATION determines the type of MEN. Not all manifestations occur within each type. Because researchers only identified the gene mutations responsible for MEN in the late 1990s, people who have this autosomal dominant disorder may not realize it runs in their families. Symptoms depend on the endocrine glands affected and the extent of the tumors or hypertrophy. The endocrinologist may suspect MEN based on the patterns of symptoms though GENETIC TESTING is necessary to confirm the mutation. Treatment is surgery to remove the tumors whenever possible, with follow-up CHEMOTHERAPY or RADIATION THERAPY. Doctors typically recommend prophylactic thyroidectomy for people who carry the gene mutation for MEN-2a or MEN-2b, to head off thyroid cancer as medullary thyroid cancer can be aggressive and is nearly certain to develop. People who have MEN require ongoing medical observation and treatment for hormonal deficiencies that result from therapies for the MEN.

See also GENETIC DISORDERS; INHERITANCE PATTERNS; POLYGLANDULAR DEFICIENCY SYNDROME; ZOLLINGER-ELLISON SYNDROME.

norepinephrine A peptide substance the adrenal medulla of the ADRENAL GLANDS and the synaptic vesicles in the NERVE endings produce. Norepinephrine functions in the body as a HORMONE, when synthesized by the adrenal medulla, and as a NEUROTRANSMITTER when synthesized by BRAIN structures or nerve cells. Norepinephrine is also a DOPAMINE precursor (substance the body uses as the basis for dopamine synthesis). Among the hormones activated in the STRESS RESPONSE HORMONAL CASCADE, norepinephrine acts on the BLOOD vessels to cause them to constrict (vasoconstriction), helping to raise BLOOD PRESSURE and centralize blood flow. It also facilitates GLYCOGEN conversion to GLUCOSE and lipid METABOLISM, activities related to glucose balance. The HYPOTHALAMUS directs the adrenal medulla, via the neurotransmitter acetylcholine, to release norepinephrine. As a neurotransmitter in the brain, norepinephrine appears to play a role in mood and emotion. Norepinephrine is also available as a pharmaceutical DRUG, used primarily to raise blood pressure in severe HYPOTENSION (low blood pressure) resulting from neurologic causes.

For further discussion of norepinephrine within the context of the endocrine system's structure and function please see the overview section, "The Endocrine System."

See also EPINEPHRINE; SHOCK.

oxytocin A peptide HORMONE the HYPOTHALAMUS synthesizes (produces) and the posterior lobe of the PITUITARY GLAND stores and releases. Oxytocin influences sexual arousal in men and women. In women, oxytocin stimulates uterine contractions during CHILDBIRTH and the milk letdown REFLEX during BREASTFEEDING. Oxytocin may have additional functions in men, including a role in SPERM production. Obstetricians may administer oxytocin as a pharmaceutical DRUG to stimulate uterine contractions to induce labor or to strengthen contractions during childbirth.

For further discussion of oxytocin within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); PROLACTIN; THYROID-STIMULATING HORMONE (TSH).

P

parathyroid glands Four small endocrine glands, somewhat orange or yellowish in color, normally located in two pairs on the back of each lobe of the THYROID GLAND. Sometimes one or more of the parathyroid glands is embedded in the tissue of the thyroid gland, which does not appear to affect either gland's ability to function. Though the thyroid gland and the parathyroid glands are physically connected, they are separate structures with distinct functions. The thyroid gland remains undisturbed if it is necessary to remove any of the parathyroid glands. However, the parathyroid glands have no structure to support them independently and cannot remain if it is necessary to remove the thyroid gland. Absence of all four parathyroid glands requires lifelong HORMONE THERAPY with PARATHYROID HORMONE supplement.

Occasionally the top two parathyroid glands are located in the neck well above the thyroid gland or the bottom two well below in the chest, a consequence of incomplete migration when the structures separate during fetal development. In the EMBRYO the top two parathyroid glands arise from the same tissue as the thyroid gland and the bottom two from the same tissue as the THYMUS. Because each parathyroid gland has its own substantial blood supply, its location is not critical for proper function.

For the significance of their function the parathyroid glands are amazingly small, with each gland ranging in size from about that of a grain of rice to that of a small pea. The parathyroid glands produce parathyroid HORMONE (also called parathormone), which is essential for proper calcium balance in the body. Calcium is essential for BONE DENSITY and STRENGTH as well as the conduction of NERVE impulses and MUSCLE contractions. The parathyroid glands continuously monitor the level of calcium in the BLOOD circulation as blood flows through them. Parathyroid hormone increases the amount of calcium in the blood circulation and exists in dynamic balance with CALCITONIN, a hormone the thyroid gland produces that increases the amount of calcium the bones absorb from the blood circulation.

Disorders of the parathyroid glands include HYPERPARATHYROIDISM (oversecretion of parathyroid hormone) and HYPOPARATHYROIDISM (undersecretion of parathyroid hormone). Either condition may result from hypertrophy (enlargement) of a parathyroid gland or from the development of an ADENOMA, a noncancerous tumor. Cancer of the parathyroid glands is very rare. Also rarely a person is born without parathyroid glands, a CONGENITAL ANOMALY with significant health consequences.

For further discussion of the parathyroid glands within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also OSTEOPOROSIS; PAGET'S DISEASE OF THE BONE.

parathyroid hormone A peptide HORMONE, also called parathormone, the PARATHYROID GLANDS secrete that regulates the level of calcium in the BLOOD circulation. Parathyroid hormone causes the bones to release calcium into the blood to meet the body's needs. Calcium is essential for the conduction of impulses among nerves and for MUSCLE contraction. Calcium helps maintain normal HEART RATE and rhythm.

Parathyroid hormone functions in dynamic balance with CALCITONIN, a hormone the THYROID GLAND produces that lowers blood calcium levels by stimulating the bones to absorb more calcium. Parathyroid hormone also enhances the activation

of vitamin D, increases the amounts of calcium the KIDNEYS retain and the intestines absorb, and increases the amount of phosphorus the kidneys excrete in the URINE.

Long-term excessive parathyroid hormone secretion (HYPERPARATHYROIDISM) leads to OSTEOPOROSIS, a condition in which there is substantial loss of BONE DENSITY and STRENGTH. Inadequate parathyroid hormone secretion (HYPOPARATHYROIDISM) results in disruptions of NERVE impulses and can cause muscle rigidity or cramping.

See also BONE; HYPERCALCEMIA; HYPOCALCEMIA.

pheochromocytoma A neuroendocrine tumor that secretes DOPAMINE, EPINEPHRINE, and NOREPINEPHRINE (collectively called catecholamines). About 90 percent of pheochromocytomas are noncancerous. Most pheochromocytomas develop in the adrenal medulla, the inner structure of the ADRENAL GLANDS, though can occur in other tissues throughout the body. About 10 percent of pheochromocytomas occur in conjunction with MULTIPLE ENDOCRINE NEOPLASIA (MEN), an inherited genetic disorder in which tumors form in numerous endocrine structures. The primary consequence of pheochromocytoma is HYPERTENSION (high BLOOD PRESSURE), which results from the excessive secretion of catecholamines. RETINOPATHY (damage to the RETINA and OPTIC NERVE in the EYE) and CARDIOMYOPATHY (enlarged and weakened HEART) may result with long-term untreated pheochromocytoma.

Symptoms and Diagnostic Path

Symptoms, aside from hypertension, often resemble those of other endocrine disorders, notably HYPERTHYROIDISM. Symptoms of pheochromocytoma may include

- rapid, irregular PULSE (TACHYCARDIA)
- rapid breathing (tachypnea) or shortness of breath (DYSPNEA)
- PALPITATIONS and ARRHYTHMIA (irregularities in the heartbeat)
- orthostatic HYPOTENSION (a sudden drop in blood pressure when rising from a seated or prone position)
- HEADACHE, often severe and persistent
- bouts of NAUSEA and VOMITING
- anxiety and inability to concentrate

The diagnostic path includes blood tests to assess blood electrolyte levels and to rule out more common causes of the symptoms such as hyperthyroidism, ELECTROCARDIOGRAM (ECG) to assess the HEART's electrical activity, and URINE tests to measure the amounts of catecholamine metabolites excreted in the urine. The endocrinologist may also conduct diagnostic imaging procedures such as MAGNETIC RESONANCE IMAGING (MRI) to detect the presence and location of the pheochromocytoma.

Treatment Options and Outlook

Surgery to remove the pheochromocytoma is nearly always the treatment of choice, as nonsurgical therapies are not very successful in controlling the tumor's activities. Adrenergic blocker medications (alpha blockers and beta blockers) can relieve many of the symptoms. Hypotension (low blood pressure) following the tumor's removal is common, with blood pressure gradually returning to normal as the body's production of catecholamines returns to normal. CHEMOTHERAPY follows surgery when the tumor is cancerous. Most people recover fully and without complications after surgery for noncancerous pheochromocytoma, though tumors may recur in people who have MEN. Recovery from malignant pheochromocytoma depends on the extent of METASTASIS.

Risk Factors and Preventive Measures

People who have MEN have significant risk for pheochromocytoma and should be alert to its symptoms. There are no measures to prevent these tumors from developing.

See also ADRENAL INSUFFICIENCY; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; SURGERY BENEFIT AND RISK ASSESSMENT.

pineal gland A small ENDOCRINE GLAND, about a quarter of an inch long, located within the BRAIN very near the HYPOTHALAMUS. The pineal gland is somewhat cone shaped and reddish in color. It produces MELATONIN, a peptide HORMONE that regulates the body's circadian (sleep–wake) cycle.

Researchers believe the pineal gland produces other hormones and has functions related to immune activity, though what they are remains unknown.

In the philosophies and traditions of Eastern medicine, the pineal gland is the metaphysical "third eye." Modern researchers have discovered that the pineal gland does in fact receive NERVE signals via the OPTIC NERVE and a structure of the hypothalamus called the suprachiasmatic nucleus (SCN). These signals influence the pineal gland's synthesis of melatonin, which slows when the external environment is light and accelerates with the external environment is dark.

Dysfunctions of the pineal gland are, as far as endocrinologists know, very rare. Some research has established a link between low melatonin levels and breast cancer, though further research continues to examine this connection. Researchers are also exploring possible connections between pineal function and insomnia (difficulty sleeping).

For further discussion of the pineal gland within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also SLEEP DISORDERS.

pituitary gland An ENDOCRINE GLAND located within the BRAIN that secretes the hormones that regulate the activity of the other endocrine structures, except the HYPOTHALAMUS, in the body. A distinctively glandular structure, gray in color and somewhat egg shaped, the pituitary gland nestles into a hollow of BONE at the base of the skull directly beneath the hypothalamus. This physical proximity makes possible a dedicated network of BLOOD vessels that carry hormones from the hypothalamus directly to the pituitary gland, allowing a continuous flow of chemical messages.

The pituitary gland has two lobes, the anterior lobe and the posterior lobe. The posterior lobe stores hormones it receives from the hypothalamus and releases them when hypothalamic signals it to do so. The anterior lobe produces hormones essential for growth and maturation. The hormones of the pituitary gland are peptide hormones. Disorders of the pituitary gland affect FERTILITY, growth, and METABOLISM.

Anterior Lobe Structure and Hormones

The anterior lobe of the pituitary gland, also called the adenohypophysis, is under the hormonal control of the hypothalamus. The hormones the anterior lobe of the pituitary gland synthesizes include

- ADRENOCORTICOTROPIN HORMONE (ACTH), which signals the ADRENAL GLANDS to release CORTISOL, EPINEPHRINE, and NOREPINEPHRINE
- GROWTH HORMONE (GH), which stimulates growth during childhood by increasing the rate at which cells divide and helps maintain MUSCLE mass in adulthood
- THYROID-STIMULATING HORMONE (TSH), which stimulates the THYROID GLAND to release the primary thyroid hormones THYROXINE (T_4) and TRIIODOTHYRONINE (T_3)
- FOLLICLE-STIMULATING HORMONE (FSH), which initiates egg maturation in the OVARIES and SPERM production in the TESTES
- LUTEINIZING HORMONE (LH), which stimulates egg release in the ovaries and TESTOSTERONE secretion from the testes
- PROLACTIN, which stimulates milk production during BREASTFEEDING

These hormones all initiate hormonal cascades among other endocrine structures. Negative-feedback loops regulate the amounts of hormones the pituitary gland secretes, with secretions slowing or stopping when terminal hormones reach appropriate levels in the blood circulation. The hormones of the anterior pituitary are integral to the body's STRESS RESPONSE HORMONAL CASCADE.

HORMONES OF THE ANTERIOR PITUITARY LOBE

ADRENOCORTICOTROPIN HORMONE (ACTH)	FOLLICLE-STIMULATING HORMONE (FSH)
LUTEINIZING HORMONE (LH)	GROWTH HORMONE (GH)
THYROID-STIMULATING HORMONE (TSH)	PROLACTIN

Posterior Lobe Structure and Hormones

The posterior lobe of the pituitary gland, also called the neurohypophysis, receives the hormones ANTIDIURETIC HORMONE (ADH) and OXYTOCIN from the hypothalamus and then stores them. The

posterior lobe does not itself synthesize any hormones. The hypothalamus regulates the posterior lobe primarily through neurologic signals (notably via the NEUROTRANSMITTER acetylcholine) that stimulate it to release its hormones into the blood circulation.

HORMONES OF THE POSTERIOR PITUITARY LOBE	
ANTIDIURETIC HORMONE (ADH)	OXYTOCIN

For further discussion of the pituitary gland within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ACROMEGALY; ADENOMA; ANABOLIC STEROIDS AND STEROID PRECURSORS; CORTICOTROPIN-RELEASING HORMONE (CRH); GONADOTROPIN-RELEASING HORMONE (GNRH); GROWTH HORMONE–RELEASING HORMONE (GHRH); HYPERPROLACTINEMIA; HYPOPITUITARISM; THYROTROPIN-RELEASING HORMONE (TRH).

polyglandular deficiency syndrome An autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack various endocrine glands and structures, resulting in deficiencies of the hormones the structures produce. The endocrine glands most commonly affected are the ADRENAL GLANDS, the THYROID GLAND, the PARATHYROID GLANDS, and the PITUITARY GLAND. When one autoimmune deficiency condition develops in an endocrine structure, others are likely to follow. The three types of polyglandular deficiency syndrome are

- type 1 polyglandular deficiency syndrome, which affects children under the age of 12 and typically affects the parathyroid glands, causing HYPOPARATHYROIDISM, and the adrenal glands, causing ADRENAL INSUFFICIENCY or ADDISON'S DISEASE
- type 2 polyglandular deficiency syndrome, which affects adults over the age of 30 and includes type 1 DIABETES, adrenal insufficiency or Addison's disease, and HYPOTHYROIDISM
- type 3 polyglandular deficiency syndrome, which affects women age 40 to 50 and includes THYROIDITIS, early MENOPAUSE, Addison's disease, and VITILIGO

Symptoms correlate to the endocrine glands affected and the endocrine disorders that result from damage to those glands. As well, symptoms may also affect functions such as FERTILITY, particularly when the thyroid gland is among the involved endocrine glands. Fertility requires a fairly precise endocrine balance throughout the body. The diagnostic path combines clinical evidence, history of symptoms, and laboratory tests that measure various HORMONE levels. All forms of polyglandular deficiency syndrome are chronic and require appropriate, lifelong HORMONE THERAPY to supplement or replace deficient hormones.

See also ANTIBODY; AUTOIMMUNE DISORDERS; ENDOCRINE GLAND; HYPERTHYROIDISM; INSULIN RESISTANCE; MULTIPLE ENDOCRINE NEOPLASIA (MEN).

progesterone A steroid HORMONE the adrenal cortex of the ADRENAL GLANDS, the OVARIES, and the TESTES synthesize from a base of cholesterol. Adipose cells (fat cells) also synthesize small amounts of progesterone. Progesterone is a precursor hormone from which men and women synthesize TESTOSTERONE. The HYPOTHALAMUS initiates the hormonal cascade that results in progesterone synthesis with the release of GONADOTROPIN-RELEASING HORMONE (GNRH), which stimulates the anterior lobe of the PITUITARY GLAND to produce LUTEINIZING HORMONE (LH) and FOLLICLE-STIMULATING HORMONE (FSH). LH and FSH act on the gonads (sex glands), stimulating their hormone productions.

Women have significantly higher levels of progesterone, which vary cyclically with MENSTRUATION, than men. In women the primary role of progesterone is to prepare the UTERUS for PREGNANCY. Progesterone levels spike with OVULATION and remain elevated for about 10 days. If pregnancy occurs, the corpus luteum continues to secrete progesterone to maintain the uterine environment. Progesterone also stimulates growth of the mammary glands in the breasts. If pregnancy does not occur the corpus luteum deteriorates, ceases progesterone production, and MENSTRUATION begins. The primary role of progesterone in men is to testosterone production.

For further discussion of progesterone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ANDROGENS; BREAST HEALTH; ESTROGENS.

prolactin A peptide HORMONE the anterior lobe of the PITUITARY GLAND synthesizes and secretes in response to the HYPOTHALAMUS's release of GONADOTROPIN-RELEASING HORMONE (GNRH). THYROID-RELEASING HORMONE (TRH) also stimulates prolactin production. Prolactin is biochemically similar to GROWTH HORMONE (GH). The primary function of prolactin is to stimulate BREAST development and milk production in women who are BREASTFEEDING. Prolactin also appears to play a role in certain immune responses. Other cells throughout the body also synthesize and secrete prolactin, which researchers believe is to enhance prolactin's immune functions. High levels of ESTROGENS in the BLOOD, such as occur near the end of PREGNANCY, increase prolactin secretion. DOPAMINE, a peptide hormone the hypothalamus secretes, signals the pituitary gland to stop secreting prolactin. Pituitary ADENOMA (a noncancerous tumor) can cause excessive prolactin secretion, resulting in galactorrhea (abnormal milk production) in men as well as women.

For further discussion of prolactin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); HYPERPROLACTINEMIA; LUTEINIZING HORMONE (LH); OXYTOCIN.

R–S

relaxin A peptide HORMONE with poorly understood roles in reproduction and CHILDBIRTH. Relaxin receptors are widespread throughout the body in both men and women. In women the OVARIES, corpus luteum, and breasts—and the PLACENTA during PREGNANCY—produce relaxin. In men, the PROSTATE GLAND and the seminal vesicles produce relaxin. Relaxin is biochemically similar to INSULIN and has numerous effects on smooth MUSCLE tissue and collagen (connective tissue) in the UTERUS, reproductive tract, cardiovascular system, urinary system, and gastrointestinal system. During pregnancy relaxin facilitates collagen remodeling, the alterations that take place in the collagen structures of the ligaments and tendons that support the enlarging uterus. During CHILDBIRTH relaxin appears to, as the name implies, relax the smooth muscles of the CERVIX and uterus after contractions. In men relaxin may facilitate the transportation of SPERM through the seminal vesicles.

For further discussion of relaxin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also CHORIONIC GONADOTROPIN; ESTROGENS; OXYTOCIN; PROLACTIN; PROGESTERONE.

renin A peptide HORMONE the KIDNEYS produce that sets in motion the sequence of events to convert angiotensinogen, an inert enzyme the LIVER stores, to angiotensin II, a potent vasoconstrictor (chemical that causes the blood vessels to narrow and stiffen, which raises BLOOD PRESSURE). Angiotensin II also stimulates the adrenal cortex of the ADRENAL GLANDS to release ALDOSTERONE. The kidneys secrete renin whenever they sense a reduction in the fluid volume in the BLOOD that passes through them. Aldosterone causes the kidneys to increase the amount of sodium they withhold from the blood, which in turn draws more water back into the blood circulation. In combination, these actions increase blood volume and blood pressure. Aldosterone's presence in the blood circulation and its actions on the kidneys also suppress renin secretion. The sequence of events is the renin–angiontensin–aldosterone (RAA) system, the body's key mechanism for regulating blood pressure and blood volume.

The RAA balance adjusts nearly continuously, as the blood's pressure and volume fluctuate with body activities down to even the most minute metabolic alterations. The release of renin may surge when a person stands up, for example, and slow when a person lies down, and even when a person transitions from sleep to wake. The RAA system relies on the proper functioning of all three component elements; dysfunction of any results in HYPERTENSION (high blood pressure). Kidney disease, particularly RENAL FAILURE, and HYPERALDOSTERONISM are the most important health conditions that influence the RAA system because both interfere with the release of renin. The excessive aldosterone in the blood circulation with hyperaldosteronism suppresses renin release, and kidney disease may interfere with the ability of the kidneys to sense fluid volume or may damage the cells that synthesize renin.

For further discussion of renin within the context of the endocrine system's structure and function, please see the overview section "The Endocrine System."

See also ANTIDIURETIC HORMONE (ADH).

somatostatin A peptide HORMONE the delta cells of the ISLETS OF LANGERHANS in the PANCREAS primarily synthesize (produce). The HYPOTHALAMUS and

the gastrointestinal tract also synthesize somatostatin. Somatostatin is an inhibitory hormone that has numerous functions related to METABOLISM and growth. It stops the release of GROWTH HORMONE (GH), INSULIN, GLUCAGON, and the DIGESTIVE HORMONES. Somatostatin also slows the activity of the gastrointestinal tract by reducing the release of acids and enzymes necessary for digestion. These actions slow the rate with which the gastrointestinal tract absorbs NUTRIENTS. Somatostatin further blocks the LIVER from converting glycogen to GLUCOSE.

Endocrinologists use an injectable pharmaceutical somatostatin preparation, octreotide, to treat ACROMEGALY, a condition that results from excessive GH production. Like endogenous somatostatin, octreotide blocks the anterior lobe of the PITUITARY GLAND from secreting GH. Type 1 DIABETES, an autoimmune disorder that destroys islet cells, often reduces the ability of the islets of Langerhans to produce somatostatin. However, the numerous other sources within the body appear capable of maintaining an adequate supply.

For further discussion of somatostatin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also AUTOIMMUNE DISORDERS; DIGESTIVE ENZYMES.

stress response hormonal cascade The hormonal responses that occur across endocrine structures to prepare the body to manage physiologic stress such as a strong increase in physical activity (for example, running). The stress response hormonal cascade begins when the HYPOTHALAMUS receives input that the body is experiencing stress. It releases a surge of CORTICOTROPIN-RELEASING HORMONE (CRH), which stimulates the anterior lobe of the PITUITARY GLAND to produce ADRENOCORTICOTROPIN HORMONE (ACTH). Concurrently the hypothalamus releases THYROTROPIN-RELEASING HORMONE (TRH), which stimulates the anterior pituitary to produce THYROID-STIMULATING HORMONE (TSH). The hypothalamus further stimulates, through neurotransmitters, the adrenal medulla to increase the release of EPINEPHRINE and NOREPINEPHRINE. These hormones stimulate NERVE cell communication such as in the muscles.

ACTH instructs the adrenal cortex of the ADRENAL GLANDS to release CORTISOL, which has numerous effects on cardiovascular and pulmonary functions. Cortisol is the body's fight-or-flight HORMONE that increases BLOOD flow to critical organs, HEART RATE, BLOOD PRESSURE, and BREATHING rate. Cortisol also stimulates the LIVER to convert glycogen to GLUCOSE, ramping up the blood supply of this essential energy source. The increase in blood glucose causes the ISLETS OF LANGERHANS to release INSULIN, which prepares cells throughout the body to receive additional glucose. TSH directs the THYROID GLAND to increase secretion of the thyroid hormones to accelerate METABOLISM, increasing cellular use of the now-available glucose supplies.

This hormonal cascade remains in action for as long as the body needs the ability to respond to the physiologic stress it faces. For the example of running, this might be until the running stops and cardiovascular and pulmonary functions return to normal levels. When the stress passes the cascades gradually reverse until the body's hormone levels also return to normal. Fear, anger, and other intense emotions also can activate the stress response hormonal cascade. Persistent activation of the stress response hormonal cascade eventually becomes dysfunctional, with the potential to cause damage to blood vessels and organ systems.

See also ALDOSTERONE; HYPERTENSION; STRESS AND STRESS MANAGEMENT.

T

testosterone A steroid HORMONE the adrenal cortex of the ADRENAL GLANDS, the TESTES in men, and the OVARIES in women synthesize from a base ingredient of cholesterol. Adipose (fat) cells throughout the body also produce small amounts of testosterone. Testosterone is one of the ANDROGENS and the predominant male sex hormone. It is responsible for male secondary sex characteristics, male FERTILITY, and spermatogenesis (SPERM production). In men and women both testosterone is important for MUSCLE mass, BONE DENSITY, and LIBIDO (sex drive).

In men testosterone levels peak around age 22, then decline at the rate of about 10 percent per decade until about age 75. Changes in a man's body shape begin to take place when the testosterone level reaches about 60 percent of its peak level, when a man is in his late 50s and early 60s. These changes include diminishing muscle mass, increased and redistributed body fat, loss of the HAIR on the head, and slower sexual response. Some men equate these midlife changes with "male MENOPAUSE" or ANDROPAUSE. In women testosterone levels cyclically fluctuate with the MENSTRUATION until menopause, after which the levels of testosterone and ESTROGENS drop significantly. Some women experience diminished sexual response as a result.

Endocrinologists may prescribe low-DOSE testosterone supplement to restore sexual response in men and women. Testosterone supplement also enhances spermatogenesis in men and may be a treatment for male INFERTILITY.

For further discussion of testosterone within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ALOPECIA; ANABOLIC STEROIDS AND STEROID PRECURSORS; HIRSUTISM; HYPOGONADISM; INHIBIN; PROGESTERONE.

thymosin A peptide HORMONE the THYMUS produces that influences how and when T-cell lymphocytes (white BLOOD cells that fight INFECTION) mature. The epithelial cells of the outer structure of the thymus synthesize thymosin most actively during childhood. Researchers do not fully understand the functions of the thymus or thymosin, particularly in adulthood. Current research is exploring the potential for using thymosin supplement to treat diseases such as HEPATITIS C and HIV/AIDS.

For further discussion of thymosin within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also IMMUNODEFICIENCY; LYMPHOCYTE.

thyroid cancer Malignant growths that develop within the tissues of the THYROID GLAND. Thyroid CANCER may be primary (originating in the thyroid gland) or secondary (metastasizing from cancer that originates elsewhere in the body). Thyroid cancer is uncommon in the United States, with about 11,000 cases diagnosed each year, and occurs primarily in people who are over age 70. There are four kinds of thyroid cancer: papillary, follicular, medullary, and anaplastic.

Papillary thyroid cancer About 75 percent of people who have thyroid cancer have papillary CARCINOMA, which is highly curable when detected and removed while the tumor is still encapsulated and clearly defined. Papillary thyroid cancer generally begins as a painless, single lump (nodule)

arising from the follicular cells and tends to grow slowly. This form of thyroid cancer is more common in people who have had previous RADIATION THERAPY to the neck, lower face, or upper chest, and in people who have autoimmune (Hashimoto's) THYROIDITIS. When papillary thyroid cancer metastasizes, it does so through the lymphatic system and usually only to adjacent lymph nodes.

Follicular thyroid cancer About 15 percent of thyroid cancers are follicular carcinomas, which also develop in the follicular cells. Follicular carcinoma does not correlate to previous radiation therapy or benign thyroid conditions. This form of thyroid cancer tends to metastasize through the BLOOD circulation, causing secondary tumors remote from the original tumor. With early detection and treatment (before METASTASIS), follicular thyroid cancer is highly curable. After metastasis, however, the prognosis declines considerably.

Medullary thyroid cancer About 8 percent of thyroid cancers are medullary carcinomas, which develop in the parafollicular cells which synthesize CALCITONIN. Consequently, excessive blood levels of calcitonin in the absence of other health conditions strongly suggest this thyroid cancer. Because these cells are less organized structurally, cancer that arises from them is less clearly delineated and accordingly more difficult to see or feel. This form of thyroid cancer often occurs in the inherited genetic disorder MULTIPLE ENDOCRINE NEOPLASIA (MEN). Rarely, medullary thyroid cancer is inherited without MEN. Medullary thyroid cancer tends to metastasize early to adjacent lymph nodes. Distant metastasis to remote sites significantly worsens the prognosis.

Anaplastic thyroid cancer About 2 percent of people who develop thyroid cancer have anaplastic carcinoma, which is the most lethal of the cancers that involve the thyroid gland. It grows rapidly and spreads aggressively. Anaplastic thyroid cancer is more likely to develop in men over the age of 70 and is very rare in people under age 50.

Symptoms and Diagnostic Path

The typical symptom of any form of thyroid cancer is a painless lump or swelling in the neck. The person may see the swelling in the mirror or feel the lump. Many times a doctor discovers a thyroid cancer during a routine medical examination or when examining the neck for other reasons. Some people experience difficulty swallowing or talking, depending on the location and size of the tumor.

The diagnostic path typically includes blood tests to measure the levels of the thyroid hormones, including THYROID-STIMULATING HORMONE (TSH), though the results may be normal. ULTRASOUND and a radioisotope iodine reuptake test can identify the tumor and provide some clues as to whether it is cancerous, though fine-needle aspiration (FNA) biopsy provides the definitive diagnosis. In FNA the endocrinologist uses a small needle and syringe to withdraw a sample of cells from the growth. Laboratory examination then determines whether the cells are cancerous, and what type of cancer is present.

Treatment Options and Outlook

For nearly all thyroid cancers, treatment is surgery to remove the thyroid gland (thyroidectomy) followed by radioactive iodine to kill any remaining thyroid cells. The radioactive iodine acts as a form of CHEMOTHERAPY and invades thyroid cells no matter where they are in the body. The exception is for medullary thyroid cancer, which arises from the parafollicular cells that do not take in iodine. The doctor may choose conventional chemotherapy or radiation therapy to follow surgery for medullary thyroid cancer. When a papillary thyroid cancer is small and contained, the doctor may feel lobectomy (removal of the involved lobe of the thyroid gland) is adequate. The decision must consider numerous factors, however, and the person who has thyroid cancer should make an informed choice based on full consideration of those factors.

Thyroid cancers detected and removed early in their development have the highest treatment success rate, and can be up to 90 percent curable (papillary and follicular). Medullary and anaplastic thyroid cancers are more difficult to diagnose in their early stages, and thus tend to be more advanced and often have metastasized by the time treatment begins. After thyroidectomy, it is necessary to take lifelong thyroid hormone supplements.

Risk Factors and Preventive Measures

The primary risk factor for papillary and anaplastic thyroid cancers is previous radiation therapy to the neck, lower face, or upper chest. Radiation exposure causes about 80 percent of papillary thyroid cancers. Family history may establish a risk for medullary thyroid cancer, as does having MEN. Risk factors for anaplastic thyroid cancer are unknown. Early diagnosis is the most effective measure for successful treatment.

See also CANCER TREATMENT OPTIONS AND DECISIONS; GOITER; SURGERY BENEFIT AND RISK ASSESSMENT; THYROID NODULE; THYROID STORM.

thyroid gland An ENDOCRINE GLAND that spreads across the front of the THROAT somewhat in the shape of a butterfly. Reddish brown in color, the thyroid gland has two lobes that equally produce the hormones CALCITONIN, THYROXINE (T_4), and TRIIODOTHYRONINE (T_3), as well as a number of precursor (inactive) thyroid hormones. The cells responsible for thyroid hormone production are the thyroid epithelial cells, also called follicular cells, which appear in clusters called thyroid follicles. The follicular cells are the only cells in the body that take in iodine, a mineral essential for thyroid hormone formation. Interspersed among the thyroid follicles are the parafollicular cells, also called C cells, which synthesize calcitonin.

The Thyroid Hormones: Metabolic Regulation

About 90 percent of the thyroid gland's hormone production is T_4, so-called because its chemical structure contains four iodine molecules. The other 10 percent is primarily T_3 (a structure of three iodine molecules) along with a number of minor hormones with unknown functions in the body. Because the thyroid hormones are not water soluble, they leave the thyroid gland attached to protein carriers the LIVER produces called thyroid-binding globulin (TBG). The TBG transports the thyroid hormones through the BLOOD to cells throughout the body.

All cells have receptors for T_3 and T_4, as these thyroid hormones regulate cellular METABOLISM (the exchange of energy within the cell). The thyroid hormones are the only peptide hormones that can pass through the cell membrane to activate receptors within the cell cytoplasm. T_3 and T_4 appear to concentrate the enzymes that regulate the transfer of energy within cells. T_3 is about 10 times more potent than T_4, though about one tenth as abundant in the blood circulation. Researchers believe that after T_4 binds with cell receptors it drops an iodine molecule to transform into the more active T_3; however, they do not understand the precise mechanisms by which this takes place. T_3 that binds with cell receptors remains T_3.

On a larger scale the thyroid hormones regulate the body's metabolism as well, controlling how the body uses energy. The thyroid hormones regulate body temperature, lipid and carbohydrate metabolism, HEART RATE, the force of the HEART's contractions, and normal growth and development. Adequate thyroid hormone levels are also necessary for FERTILITY (HYPOTHYROIDISM is one of the most common causes of INFERTILITY) and for cognitive function.

Thyroid hormones are critical for normal BRAIN development in the unborn child as well as throughout childhood. Rarely a child is born without a thyroid gland or with a severely dysfunctional thyroid gland. This establishes congenital hypothyroidism, formerly called cretinism, a syndrome of pronounced growth and intellectual deficits. The damage is permanent without immediate HORMONE THERAPY to provide the body with the necessary thyroid hormones. Undetected fetal hypothyroidism results in permanent damage to the brain, NERVOUS SYSTEM, and other organ systems and structures. Congenital hypothyroidism is rare in the United States because routine newborn and child health-care standards include regular screening for thyroid hormone levels.

Calcitonin: Bone Density and Calcium Balance

The parafollicular cells of the thyroid gland produce the peptide hormone calcitonin, which regulates the balance of calcium and phosphorus in the bones and blood. The thyroid gland releases calcitonin in response to elevated levels of calcium in the blood. Calcitonin binds with receptors in the KIDNEYS, increasing the amount of phosphorus excreted into the URINE, and in osteoblasts (cells within the bones that create new BONE tissue), stimulating them to accept calcium. Calcitonin functions in dynamic balance with PARATHYROID

HORMONE, which draws calcium from the bones into the blood to meet the calcium needs elsewhere in the body.

Generally, disorders of the thyroid gland have little effect on calcitonin synthesis because such disorders affect the follicular cells. A notable exception is an uncommon form of THYROID CANCER called medullary carcinoma, which develops in the parafollicular cells that synthesize calcitonin. Elevated levels of calcitonin in the blood circulation without corresponding parathyroid dysfunction raise the suspicion that such a cancer is present.

COMMON DISORDERS OF THE THYROID GLAND

GOITER	GRAVES'S DISEASE
HYPERTHYROIDISM	HYPOTHYROIDISM
POLYGLANDULAR DEFICIENCY SYNDROME	THYROID CANCER
THYROIDITIS	THYROID NODULE
THYROID STORM	

For further discussion of the thyroid gland within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also AGING, ENDOCRINE CHANGES THAT OCCUR WITH; HYPERCALCEMIA; HYPERPARATHYROIDISM; HYPOCALCEMIA; HYPOPARATHYROIDISM.

thyroiditis INFLAMMATION of the follicular cells of the THYROID GLAND. The inflammation prevents these cells from synthesizing thyroid hormones, resulting in HYPOTHYROIDISM. In some forms of thyroiditis the inflammation resolves and the follicular tissue returns to normal thyroid HORMONE production. In other forms the inflammation heals but forms SCAR tissue (fibrosis), permanently destroying the ability of the affected follicular cells to synthesize thyroid hormones. Thyroiditis does not affect the parafollicular cells in the thyroid gland that produce CALCITONIN.

The three main types of thyroiditis are

- autoimmune thyroiditis, sometimes called Hashimoto's thyroiditis or chronic lymphocytic thyroiditis, which often develops in people who have other AUTOIMMUNE DISORDERS and is the most common type of thyroiditis
- silent thyroiditis, which often develops in women who have recently given birth and generally begins with HYPERTHYROIDISM
- subacute thyroiditis, also called granulomatous thyroiditis or subacute lymphocytic thyroiditis, which typically develops after a viral INFECTION

Other rare types of thyroiditis include Reidel's thyroiditis, in which the thyroid becomes fibrotic

THYROIDITIS SYMPTOMS AND TREATMENT

Autoimmune (Hashimoto's) Thyroiditis	Silent Thyroiditis	Subacute Thyroiditis
no PAIN	no pain	pain
gradual hypothyroid onset: progressive fatigue, weight gain, mild GOITER	hyperthyroid onset within four months of CHILDBIRTH: weight loss, anxiety, insomnia, agitation	rapid hyperthyroid onset: weight loss, anxiety, insomnia, agitation
permanent destruction of thyroid follicular cells	no treatment for HYPERTHYROIDISM because duration is short	transition to hypothyroid: weight gain, fatigue, lethargy
permanent HYPOTHYROIDISM with lifelong thyroid supplement HORMONE THERAPY	transition to hypothyroid eight months after childbirth: weight gain, fatigue, lethargy, DEPRESSION	swelling and tenderness of neck
	damage to thyroid follicular cells often permanent, with resulting permanent hypothyroidism	NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) may relieve pain and some INFLAMMATION
	lifelong thyroid supplement hormone therapy	THYROID GLAND often fully recovers and no treatment is necessary
		permanent hypothyroidism requires lifelong thyroid supplement hormone therapy

(scarred) and merges with surrounding structures, and acute thyroiditis, which is a serious and potentially life-threatening bacterial infection of the thyroid gland that requires emergency medical treatment.

Symptoms and Diagnostic Path

Sometimes the first indications of thyroiditis are the symptoms of hyperthyroidism, as the inflammation causes the follicular cells to release a surge of thyroid hormones into the BLOOD circulation. When the effect of this surge subsides thyroid hormone levels in the blood drop below normal, establishing a state of hypothyroidism. The diagnostic path begins with blood tests to measure thyroid hormone and ANTIBODY levels, and may include diagnostic imaging procedures such as ULTRASOUND or radioisotope iodine reuptake test to further evaluate thyroid function and the presence of any nodules or swelling.

Treatment Options and Outlook

When thyroid symptoms are transitory, as with silent thyroiditis and often with subacute thyroiditis, HORMONE THERAPY with thyroid supplement is not necessary. Nor is it necessary to treat the hyperthyroid phase, because this is typically of short duration. Lifelong thyroid supplement hormone therapy becomes necessary when scarring permanently destroys thyroid follicular cells.

Risk Factors and Preventive Measures

The primary risk for autoimmune thyroiditis is the existence of any other autoimmune disorders. Silent thyroiditis nearly always follows CHILDBIRTH, and subacute thyroiditis follows a viral infection. Knowing of these risks increases the chance of early diagnosis, which can minimize the course of the duration. However, there are no preventive measures for thyroiditis.

See also GRAVES'S DISEASE; THYROID CANCER; THYROID NODULE; THYROID STORM.

thyroid nodule A small growth that develops within the tissues of the THYROID GLAND. Most thyroid nodules (about 90 percent) are noncancerous. Thyroid nodules, like other thyroid disorders, are significantly more common in women than men and become increasingly common with advancing age. Endocrinologists call a thyroid nodule "hot" when its tissue secretes thyroid hormones and "cold" when it does not. Most malignant (cancerous) thyroid nodules are cold, while nearly all hot nodules are benign (noncancerous).

Most thyroid nodules do not cause symptoms. The person may notice a lump on the front of the neck when looking in the mirror. Often the doctor detects a thyroid nodule during a ROUTINE MEDICAL EXAMINATION. Thyroid nodules may oversecrete thyroid hormones, resulting in symptoms of HYPERTHYROIDISM. The diagnostic path may include ULTRASOUND examination of the neck and a radioisotope iodine reuptake test, which measures the ability of the nodule to take in iodine. Normal thyroid tissue uses iodine to synthesize thyroid hormones. A nodule composed of tissue other than thyroid tissue (a cold nodule) does not take up iodine. A fine-needle aspiration (FNA) biopsy, in which the endocrinologist withdraws a small tissue sample from the nodule using a thin needle and a syringe, provides cells for laboratory examination to determine whether the nodule is cancerous. A single node is more suspicious than are multiple nodes.

Some thyroid nodules resolve on their own without treatment. The endocrinologist may prefer to surgically remove a thyroid nodule that is causing symptoms, including those of hyperthyroidism, or that is growing though often chooses a course of watchful waiting for asymptomatic nodules that biopsy negative for CANCER and are not growing. Thyroid nodules may occur in THYROIDITIS (INFLAMMATION of the thyroid gland) or HYPOTHYROIDISM (underactive thyroid gland).

See also AGING, ENDOCRINE CHANGES THAT OCCUR WITH; GOITER; THYROID CANCER.

thyroid-stimulating hormone (TSH) A peptide HORMONE the anterior lobe of the PITUITARY GLAND synthesizes in response to the HYPOTHALAMUS's production of THYROTROPIN-RELEASING HORMONE (TRH). TSH subsequently binds with TSH receptors on the follicular cells in the THYROID GLAND, stimulating them to synthesize the primary thyroid hormones TRIIODOTHYRONINE (T_3) and THYROXINE (T_4), as well as a number of minor or precursor hormones. TSH also influences the pituitary gland's secretion of PROLACTIN and GROWTH HORMONE (GH). TSH levels in

the blood may remain artificially high in HYPOTHYROIDISM, as the levels of thyroid hormones are chronically inadequate in this condition of underactive thyroid gland. TSH levels may be normal or low in HYPERTHYROIDISM (overactive thyroid gland), depending on the cause of the oversecretion of thyroid hormones.

For further discussion of TSH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ADRENOCORTICOTROPIN HORMONE (ACTH); ANTIDIURETIC HORMONE (ADH); FOLLICLE-STIMULATING HORMONE (FSH); GROWTH HORMONE (GH); LUTEINIZING HORMONE (LH); OXYTOCIN; PARATHYROID GLANDS; PARATHYROID HORMONE.

thyroid storm A rare but life-threatening condition resulting from HYPERTHYROIDISM in which the body experiences an exaggerated response to the overproduction of thyroid hormones.

Thyroid storm is a medical emergency that requires rapid treatment.

Thyroid storm generates severe ARRHYTHMIA and tachycardia (disturbances of the HEART's electrical activity), high FEVER (disruption of the body's heat regulation mechanisms), congestive HEART FAILURE, significant electrolyte imbalances, and seizures or psychotic behaviors. Typically thyroid storm develops when a person who has undiagnosed hyperthyroidism, most commonly the result of GRAVES'S DISEASE, experiences physiologic stress such as INFECTION, trauma, or surgery. The circulating thyroid hormones overwhelm the cells, dramatically accelerating METABOLISM. The body's usual negative-feedback loop mechanisms fail, and the THYROID GLAND continues to pour thyroid hormones into the BLOOD circulation.

Symptoms and Diagnostic Path

The symptoms and signs of thyroid storm manifest rapidly and include

- severe NAUSEA, VOMITING, and DIARRHEA
- high fever (above 105°F)
- confusion and anxiety
- DYSPNEA (difficulty BREATHING) and TACHYPNEA (rapid breathing)
- racing or pounding PULSE (140 beats per minute or greater)

The diagnostic path begins with blood tests to measure the levels of thyroid hormones. Typically, THYROXINE (T_4) and TRIIODOTHYRONINE (T_3) are significantly elevated and THYROID-STIMULATING HORMONE (TSH) is low. However, the diagnosis is primarily clinical (based on signs and symptoms).

Treatment Options and Outlook

Treatment aims to bring thyroid hormone levels down as quickly as possible, usually with the medications methimazole or propylthiouracil (PTU). Follow-up administration of intravenous iodine blocks the thyroid gland from resuming thyroid hormone production. Plasmapheresis to filter thyroid hormones from the blood may be a treatment option for people who do not respond to these measures. Beta blocker medications such as propanolol help thwart the actions of thyroid hormones that reach cells throughout the body. Other therapies target symptoms, such as cooling to bring the body temperature down and medications to regulate the heart's rhythm. Once the person's status stabilizes, the endocrinologist typically begins treatment for the underlying hyperthyroidism, which may include surgery to remove the thyroid gland or radioactive iodine to destroy the thyroid gland's ability to produce thyroid hormones.

Without treatment, or when treatment begins too late, thyroid storm is fatal. With appropriate and timely treatment about 80 percent of people who experience thyroid storm survive. After treatment, lifelong HORMONE THERAPY with thyroid hormone supplement is necessary.

Risk Factors and Preventive Measures

The primary risk factor for thyroid storm is undiagnosed hyperthyroidism. Appropriate treatment for hyperthyroidism can eliminate the risk for thyroid storm.

See also HYPOTHYROIDISM; THYROIDITIS.

thyrotoxicosis See HYPERTHYROIDISM.

thyrotropin-releasing hormone (TRH) A peptide HORMONE the HYPOTHALAMUS produces in response to decreased levels of the thyroid hormones in the BLOOD circulation. TRH initiates the hormonal cascade that regulates the synthesis and release of thyroid hormones from the THYROID GLAND. TRH stimulate the anterior lobe of the PITUITARY GLAND to release THYROID-STIMULATING HORMONE (TSH). TSH in turn binds with TSH receptors on the surface of the follicular cells in the THYROID GLAND, stimulating them to produce TRIIODOTHYRONINE (T_3) and THYROXINE (T_4), the primary thyroid hormones. Increased levels of T_3 and T_4 in the blood circulation signal the hypothalamus to "turn off" TRH secretion.

For further discussion of TRH within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also ANTIDIURETIC HORMONE (ADH); CORTICOTROPIN-RELEASING HORMONE (CRH); GONADOTROPIN-RELEASING HORMONE (GNRH); GROWTH HORMONE–RELEASING HORMONE (GHRH).

thyroxine (T_4) A peptide HORMONE the THYROID GLAND synthesizes from iodine and the amino acid tyrosine, both of which enter the body from dietary sources. The follicular cells in the thyroid gland synthesize T_4. Thyroxine is designated T_4 because its chemical structure contains four iodine molecules (as well as two tyrosine molecules). About 80 percent of the thyroid gland's hormone production is T_4. T_4 travels through the blood circulation bound to the protein carrier thyroxine-binding globulin (TBG), which the LIVER synthesizes. All cells in the body have receptors for T_4, which passes across the cell membrane (cell wall) to bind with receptors in the cell cytoplasm. Upon binding T_4 appears to drop an iodine molecule to become the more potent TRIIODOTHYRONINE (T_3). In combination, T_3 and T_4 regulate cellular METABOLISM (the conversion of energy within cells).

The HYPOTHALAMUS regulates the thyroid hormone cascade, which it initiates by producing THYROTROPIN-RELEASING HORMONE (TRH). TRH stimulates the anterior lobe of the PITUITARY GLAND to secrete THYROID-STIMULATING HORMONE (TSH). TSH, in turn, stimulates the thyroid gland to synthesize and release T_4 (as well as T_3). An underactive thyroid gland produces inadequate amounts of T_3 and T_4, resulting in HYPOTHYROIDISM and slowed metabolism. An overactive thyroid gland produces too much T_3 and T_4, resulting in HYPERTHYROIDISM and an accelerated metabolic rate. T_4 is the most common ingredient in thyroid hormone supplements.

For further discussion of T_4 within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also THYROIDITIS; THYROID STORM.

triiodothyronine (T_3) A peptide HORMONE the THYROID GLAND synthesizes from iodine and the amino acid tyrosine, both of which the body acquires through dietary sources. The follicular cells in the thyroid gland synthesize T_3. Triiodothyronine is designated T_3 because its chemical structure contains three iodine molecules in addition to two tyrosine molecules. About 20 percent of the thyroid gland's hormone production is T_3. T_3 is about 10 times more potent than THYROXINE (T_4), the other major thyroid hormone. All cells in the body have receptors for T_3, which passes across the cell membrane (cell wall) to bind with those receptors within the cell cytoplasm. T_3 then directly influences the cell's DNA, guiding its production of proteins. In combination, T_3 and T_4 regulate cellular METABOLISM.

The HYPOTHALAMUS regulates the thyroid hormone cascade, which it initiates by producing THYROTROPIN-RELEASING HORMONE (TRH). TRH stimulates the anterior lobe of the PITUITARY GLAND to secrete THYROID-STIMULATING HORMONE (TSH). TSH, in turn, stimulates the thyroid gland to synthesize and release T_3 (as well as T_4). An underactive thyroid gland produces inadequate amounts of T_3 and T_4, resulting in HYPOTHYROIDISM and slowed metabolism. An overactive thyroid gland produces too much T_3 and T_4, resulting in HYPERTHYROIDISM and an accelerated metabolic rate. T_3 is sometimes an ingredient in thyroid hormone supplements.

For further discussion of T_3 within the context of the endocrine system's structure and function please see the overview section "The Endocrine System."

See also THYROIDITIS; THYROID STORM.

V–W

vasoactive intestinal peptide (VIP) See DIGESTIVE HORMONES.

Wilson's disease A hereditary disorder in which the body does not properly metabolize copper, which allows deposits of copper to accumulate in various organs. Without treatment Wilson's disease is fatal; with treatment it is easily manageable.

Copper is an important mineral for the body's production of various enzymes, including those that facilitate HEMOGLOBIN synthesis. However, the body needs only a very small quantity of copper. In health the LIVER discharges excess copper, which enters the body through dietary sources, into the BILE. The bile carries the copper into the gastrointestinal tract for removal from the body in the feces. The KIDNEYS also extract some copper from the BLOOD circulation, passing it from the body in the URINE. In Wilson's disease a genetic MUTATION prevents the liver from discharging excess copper. Instead, it stores copper within its own tissues as well as sends it back out into the blood circulation. The blood deposits the copper in tissues throughout the body. As the copper accumulates, it causes scarring and other damage that interferes with the normal functions of the tissues.

Symptoms and Diagnostic Path

The symptoms of Wilson's disease vary according to the body system most severely affected, which is most often the liver or the BRAIN and SPINAL CORD. Liver involvement produces symptoms such as

- JAUNDICE (yellowish color to the SKIN)
- HEPATOMEGALY (enlarged liver) and SPLENOMEGALY (enlarged SPLEEN)
- ASCITES (fluid accumulation in the abdomen)
- NAUSEA and VOMITING
- abdominal discomfort or PAIN

Involvement of the brain, spinal cord, and other structures of the NERVOUS SYSTEM produces symptoms that may include

- difficulty moving the arms and legs
- tremors
- confusion
- difficulty speaking and swallowing
- cognitive and memory dysfunction

A conclusive clinical sign for Wilson's disease is the appearance of a copper-colored ring around the iris of the EYE, called a Kayser-Fleischer ring. Other diagnostic indications include low levels of copper in the blood and high levels of copper in the urine. Biopsy of the liver or the kidneys shows the copper deposits in the tissues.

Treatment Options and Outlook

Treatment targets blocking the body's absorption of copper as well as removal of excessive copper already in the body (chelation). Commonly used chelation agents include penicillamine and trientine. These drugs bind with the copper, allowing the kidneys to excrete the bound molecules from the body in the urine. Zinc acetate can help reduce gastrointestinal absorption of copper from the diet. Doctors recommend eating foods that are low in copper. People who have Wilson's disease should drink bottled water because copper is common in household plumbing and should avoid cooking with copper pans or implements. The endocrinologist may also recommend a zinc supplement, as zinc interferes with copper absorption.

FOODS HIGH IN COPPER

avocado
chocolate
dried fruits: apricots, figs, nectarines, raisins
energy bars and drinks
legumes: black beans, garbanzo beans, kidney beans, lentils, navy beans, pinto beans, peanuts, soybeans, split peas
mushrooms
nuts: almonds, cashews, hazelnuts, macadamia, pecans, walnuts
organ meats: gizzard, heart, liver, kidney
shellfish: clams, mussels, oysters, scallops, shrimp
whole grains: barley, bran

Risk Factors and Preventive Measures

Wilson's disease occurs as a result of autosomal recessive GENE mutation. People with a family history of Wilson's disease can undergo GENETIC TESTING for this mutation. Minimizing copper intake prevents excessive accumulation and its resultant damage and symptoms. Damage that has already occurred at the time of diagnosis is often permanent.

See also COGNITIVE FUNCTION AND DYSFUNCTION; GENETIC DISORDERS; HEMATOCHROMATOSIS; INHERITANCE PATTERNS; MEMORY AND MEMORY IMPAIRMENT; PHENYLKETONURIA (PKU).

THE URINARY SYSTEM

The urinary system cleanses metabolic wastes and toxins from the blood. Physician specialists who treat conditions of the urinary system are urologists (surgeons) and nephrologists (internists). This section, "The Urinary System," presents a discussion of the organs and structures of the urinary system, an overview of urinary and renal health and disorders, and entries about the health conditions that involve the urinary system.

Structures of the Urinary System

KIDNEYS
- cortex
- medulla
- renal pelvis

NEPHRON
- ureters

BLADDER

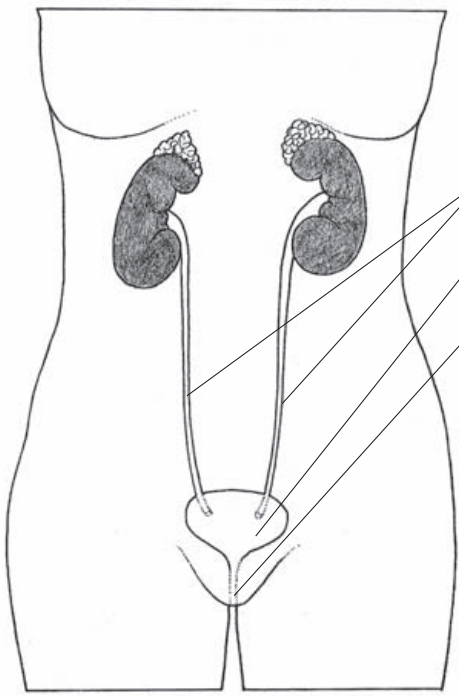
URETHRA

Functions of the Urinary System

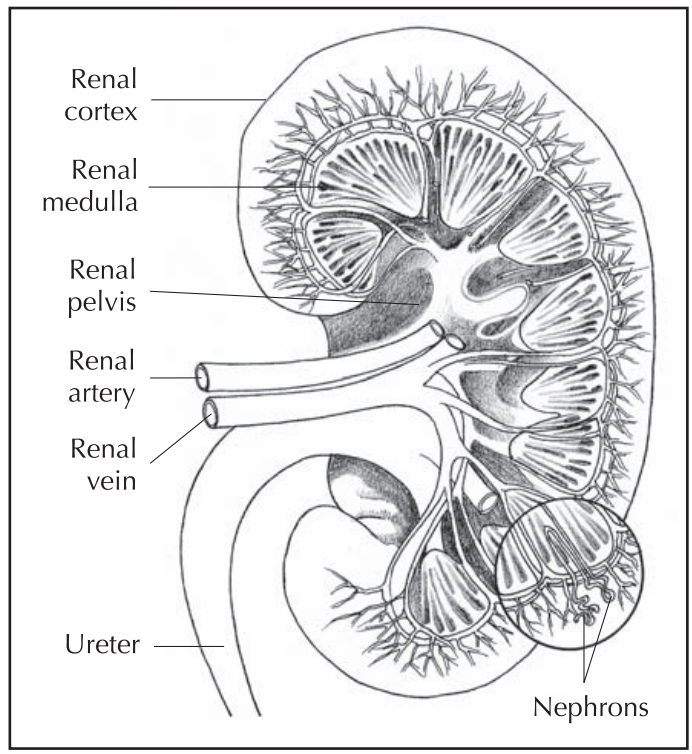
The primary functions of the urinary system's organs and structures are to filter and excrete wastes from the BLOOD and to maintain the body's fluid and electrolyte balances. The KIDNEYS make, and the bladder contains and then excretes, urine, a watery fluid that carries dissolved and suspended wastes from the body. As well, the KIDNEYS produce two essential hormones: RENIN, which helps regulate BLOOD PRESSURE, and ERYTHROPOIETIN (EPO), which stimulates the BONE MARROW to produce erythrocytes (red blood cells). The kidneys also convert vitamin D from its inactive dietary form to its active form as the HORMONE calcitriol, which is necessary for proper calcium absorption.

The kidneys: cleansing the blood The paired KIDNEYS reside in the upper posterior abdomen, behind the peritoneum along the spine and within the protection of the rib cage. The kidneys are slightly offset from one another in the symmetry of their positioning, with the right kidney being about an inch lower than the left to accommodate the LIVER. Each kidney is about the size of a man's fist, shaped like the bean that bears its name. The dark reddish brown kidneys curve toward each other, turning their backs to the body's sides. Though the kidneys have a combined weight of about 10 ounces, they hold 20 percent of the body's blood supply. The renal arteries branch directly from the abdominal AORTA, ensuring that the kidneys are among the first of the organs to receive blood with each contraction of the HEART. The renal veins channel blood returning to the circulation from the kidneys directly to the inferior VENA CAVA.

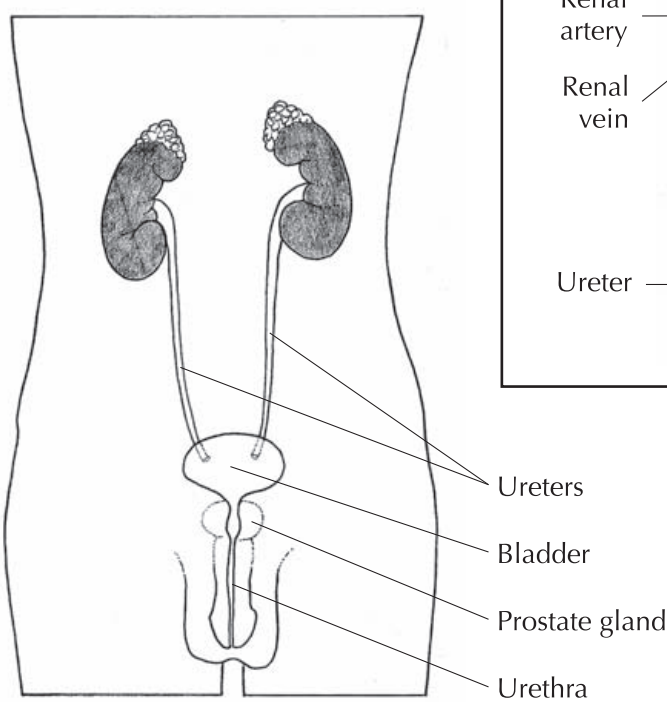
The kidney's structure features two general divisions. The outer layer is the renal cortex, intensely vascular tissue where the filtration of blood takes place. The inner layer is the renal medulla, where URINE collects. The workhorse structure of the kidney is the microscopic NEPHRON, which is made up of two elements: the renal corpuscle, contained in the renal cortex, and the tubule, contained in the renal medulla. The renal corpuscle consists of a containment capsule (called Bowman's capsule) that encloses the GLOMERULUS, a tightly coiled capillary network that receives blood from the body for filtration. The space between the inner wall of Bowman's capsule and the walls of the glomerulus collects the molecules of water, electrolytes, and metabolic wastes that pass from the blood, forming a mixture called the filtrate. The tubule is a loosely coiled structure that wraps around the renal corpuscle. It reabsorbs electrolytes and water the body needs from the filtrate and sends the remainder on with the wastes to become urine. Each tubule is about 1.25 inches in total length; were a kidney's tubules removed and stretched



Female



Kidney



Male

end to end in a straight line, they would cover more than 50 miles.

RENAL DIALYSIS: MACHINES TO CLEANSE THE BODY WHEN THE KIDNEYS CANNOT

Researchers began working in the 1920s to develop a safe, effective substitute to cleanse metabolic wastes from the BLOOD when the KIDNEYS failed. By the early 1950s such a substitute—the hemodialysis machine—entered clinical use. And by the 1970s hemodialysis was the standard treatment for END-STAGE RENAL DISEASE (ESRD). Today nearly 300,000 Americans rely on hemodialysis.

The kidneys and blood pressure The kidneys regulate blood pressure by controlling the volume of the blood and through the production of the hormone renin, which is the cornerstone of the body's RENIN–ALDOSTERONE–angiotensin (RAA) system for regulating blood pressure. Renin and aldosterone initiate chemical actions that result in constricting blood vessels and increasing blood volume to raise blood pressure.

The tubules in the nephrons continuously adjust the amounts of sodium, potassium, and chloride they reabsorb from the filtrate. Where goes the electrolytes, so goes the water. The more of electrolytes the tubules draw back into the blood, the higher the amount of water that follows. Increased reabsorption increases blood volume and raises blood pressure. Decreased reabsorption sends the electrolytes in the filtrate, along with the water that they draw, out of the body in the urine to drop both blood volume and blood pressure.

Within each nephron, where the distal tubule and the afferent arteriole (the blood vessel that brings blood into the glomerulus) nearly touch, are two clusters of specialized sensory cells. The macula densa resides within the walls of the distal tubule; its cells sense the concentration of electrolytes, primarily sodium, in the filtrate. In the interstitial space between the distal tubule and the afferent arteriole are the juxtaglomerular cells, which sense the pressure of the blood as it courses through the afferent arteriole.

The clusters are in constant communication with one another, using chemical signals to regulate how much electrolytes and water the tubules reabsorb from the filtrate. As well, these cell clusters send a continuous barrage of NERVE signals to the brainstem, which just as continuously determines the adjustments in renin release necessary to maintain the blood pressure at the level the body needs. Renin sets in motion the cascade of chemical events that converts the inactive protein angiotensinogen (also called angiotensin I) into the very potent vasoconstrictor (chemical that causes the blood vessels to narrow and stiffen, raising blood pressure) angiotensin II. Angiotensin I causes the peripheral arterioles to constrict.

Angiotensin II also signals the adrenal cortex of the ADRENAL GLANDS to release ALDOSTERONE, a hormone that stimulates the tubule to pull even more sodium (and, of course, water) back into the blood from the filtrate. The result is a rise in blood pressure. The brainstem also instructs the HYPOTHALAMUS to release ANTIDIURETIC HORMONE (ADH) when blood volume and pressure fall below a certain threshold and to withhold ADH when blood volume is above that threshold. The threshold varies with the body's activities, and the cascade of actions is a process of perpetual adjustment.

Doctors take advantage of these mechanisms to treat HYPERTENSION (high blood pressure). Diuretic medications—"water pills"—act on the tubules to block them from reabsorbing sodium and chloride. This increases the amount of water in the filtrate, preventing the tubules from increasing blood volume. Various antihypertensive medications, such as angiotensin-converting enzyme (ACE) inhibitors, target different stages of the angiotensin conversion process.

The kidneys and fluid balance The processes of the kidney that regulate blood pressure also maintain the body's fluid and electrolyte balances. The hypothalamus monitors the amount of water in the body, using ADH as the chemical messenger that tells the kidneys the body needs more water or less water.

The kidneys and erythropoiesis It seems a bit odd, at first, that the kidneys produce the hormone that stimulates the bone marrow to produce new erythrocytes (red blood cells). But no other organs have such intimate exposure to the blood that they can literally "examine" each cell. With every heartbeat 20 percent of the body's blood

volume surges through the kidneys. This blood disperses among the million or so glomeruli, the microscopic capillaries within the nephrons. Specialized sensors in the walls of the glomeruli detect the levels of oxygen in the erythrocytes as they pass by. Low levels of oxygen stimulate the kidneys to synthesize (produce and release) EPO. EPO travels through the blood circulation to the bone marrow, where it stimulates the production of new erythrocytes (erythropoiesis).

Erythropoiesis suffers in RENAL FAILURE because the blood cannot circulate through the glomeruli, resulting in ANEMIA. This is why people who have renal failure feel so fatigued. And erythropoiesis comes to a near-halt in ESRD, when the kidneys no longer function at all. Not only do toxins accumulate in the blood when the kidneys fail but also the blood cannot deliver enough oxygen because it does have enough red blood cells to carry the load. Many people who have renal failure take EPO supplement, a product of RECOMBINANT DNA technology, to maintain adequate erythropoiesis.

The kidneys and bone health Mention *strong bones* and the first association is likely to be "calcium." It might just as well be calcitriol, the hormone form of vitamin D, because without calcitriol, the body cannot use the calcium it receives. The kidneys convert dietary vitamin D, a fat-soluble vitamin inert within the body in its dietary form, to calcitriol. The kidneys further participate in the body's calcium balance because they determine how much calcium to reabsorb from the filtrate and return to the blood circulation.

Calcium is essential for numerous body activities ranging from HEALING and cell repair to nerve and MUSCLE cell communication. Calcium makes it possible to walk across the room, from the SKELETON that supports the body to the nerve impulses that instruct muscle fibers from heart to soles to contract. People who have chronic renal failure and other forms of chronic renal disease often take vitamin D supplement (calciferol). Adequate vitamin D is essential for appropriate growth in children; without it there is no growth. PARATHYROID HORMONE acts on the distal tubule to increase the amount of calcium the tubule reabsorbs.

The kidneys and urine production This most familiar and seemingly simple function of the kidneys is, of course, its most important. Without the urine to carry metabolic wastes from the blood, none of the kidney's other functions would be necessary for very long. Urine is a mixture of the water, electrolytes, and metabolic wastes (primarily urea) the kidneys extract from the blood. As blood passes through the glomerulus pressure squeezes much of the blood's water, along with electrolytes and wastes, through the glomerular walls into Bowman's capsule. This mixture, the filtrate, collects in the capsule and drains into the tubule. The tubule reabsorbs about two thirds of the water and electrolytes, passing on the remainder to become urine. Collecting tubules carry the urine into the renal pelvis, where it drains into the ureters that then channel it to the BLADDER.

Holding the urine: the bladder Suspended in the lower pelvis is the bladder, an expandable muscular sac that collects the urine that drains from the kidneys. When empty the bladder is about the size of a lemon; when filled to its capacity of about 500 milliliters the bladder is about the size of a cantaloupe. Its three-layer wall consists of a mucous inner layer, middle layer of smooth muscle, and fibrous membrane outer layer. The middle layer, called the detrusor muscle, relaxes to allow the bladder to distend when filling with urine and contracts to push urine from the bladder into the URETHRA for passage from the body.

The bladder holds the urine in a more colloquial sense as well, allowing conscious override of the micturition REFLEX, an involuntary function of the sympathetic NERVOUS SYSTEM, that initiates URINATION. At about two or three years of age the brain, muscles, and nerves have matured enough for conscious control to take over certain involuntary functions. Voluntary urination—toilet training—is the hallmark of this effort and marks the rite of passage from baby to child. Voluntary control of urination uses certain centers in the brain in coordination with voluntary muscles such as the pubococcygeal muscle to manage the timing of urination, though if the bladder becomes too full the micturition reflex becomes too intense for conscious control to overcome.

Tubes of urine transport: the ureters and urethra From each kidney a thin muscular tube drops about 12 inches to join with the bladder. Urine trickles from the kidney's collecting tubules into the renal pelvis, a deltalike structure that

channels the urine toward the URETER, which will carry the urine, like a drain, into the bladder. Though small in diameter the ureter has relatively thick, sturdy walls that contract in rhythmic waves to move urine in a steady flow. The ureter's peristaltic action also helps prevent urine from flowing back up into the kidney. Each ureter inserts into the back of the bladder wall, tunneling through the detrusor muscle for a short distance before emerging into the urothelium (inner epithelial layer of the bladder). The tunnel is another safeguard to keep urine from backflowing to the kidney, flattening unless pressure from flowing urine causes it to open.

The urethra carries urine from the base of the bladder to outside the body. A woman's urethra is less than two inches long and exits her body between the CLITORIS and the VAGINA. A man's urethra is about eight inches long and exits his body at the tip of the PENIS. A ring of muscle, the urethral sphincter, encircles the urethra at the neck of the bladder. When contracted the sphincter holds the urethra closed and urine remains in the bladder; when relaxed the sphincter allows the urethra to open and urine to leave the bladder.

Health and Disorders of the Urinary System

The kidneys have remarkable capacity. Each kidney contains more than a million nephrons. Though the normal design of the human body features two kidneys, one healthy kidney is perfectly able to meet the needs of the body. The kidneys can lose as much as 65 to 70 percent of their ability to function and still maintain the health of the body. When kidney function reaches 25 percent, however, the filtration workload overwhelms the nephrons and symptoms of kidney failure begin to manifest. And when kidney function drops to 15 percent or lower, the kidneys can no longer perform at a level that sustains life.

The most significant health challenges that confront the kidneys are DIABETES and hypertension, which are especially dangerous when they occur in combination as they do in about half of people who have diabetes as hypertension is a complication of diabetes. These two conditions place inordinate stress on the glomeruli, hypertension because it increases the pressure under which blood enters the glomeruli and diabetes because the elevated levels of GLUCOSE in the blood damage capillaries throughout the body. The glomeruli, being among the most intensely concentrated capillary networks in the body, bear the brunt of such damage. About 20 million Americans live with some degree of kidney failure and another 10 million are at risk of kidney failure because of health conditions such as diabetes and hypertension as well as conditions that directly affect the kidneys.

HEALTH CONDITIONS THAT AFFECT THE URINARY SYSTEM

ALPORT'S SYNDROME	BLADDER CANCER
BLADDER EXSTROPHY	CYSTINURIA
CYSTITIS	CYSTOCELE
END-STAGE RENAL DISEASE (ESRD)	EPISPADIAS
FANCONI'S SYNDROME	GLOMERULONEPHRITIS
GLOMERULOSCLEROSIS	GOODPASTURE'S SYNDROME
HEMOLYTIC UREMIC SYNDROME	HEPATORENAL FAILURE
HORSESHOE KIDNEY	HYDRONEPHROSIS
HYPOSPADIAS	NEPHRITIS
NEPHROLITHIASIS	NEPHROPATHY
NEPHROTIC SYNDROME	POLYCYSTIC KIDNEY DISEASE
RENAL CANCER	RENAL CYST
RENAL FAILURE	RENAL TUBULAR ACIDOSIS
UREMIA	URETHRAL STRICTURE
URETHRITIS	URINARY INCONTINENCE
URINARY TRACT INFECTION (UTI)	UROLITHIASIS
VESICOURETERAL REFLUX	WILMS'S TUMOR

Traditions in Medical History

Among the earliest known medical treatments are those for kidney stones and bladder stones. Ancient healers across cultures documented various remedies, including surgical removal, for the painful conditions known today as NEPHROLITHIASIS and UROLITHIASIS, respectively. Though early physicians could not examine the urinary structures themselves in any great detail, these structures abundantly produced a substance that many physicians turned into a diagnostic oracle: the urine. The gifted physician was one who could study the color, cloudiness, consistency, odor, and even taste of the urine to diagnose conditions ranging from HEART FAILURE to PREGNANCY to SYPHILIS and, of course, diabetes. This was the practice of uroscopy, the forerunner of modern urinalysis.

Greek philosopher and scientist Aristotle (384–322 B.C.E.), whose father was a physician,

described the urinary system's basic structure and function in his writings. However, nearly 2000 years would pass before one of science's most significant inventions, the light microscope, would give 17th-century scientists the opportunity to explore the amazing structure and function of the kidney beyond the human EYE's ability to detect. Advances in modern times such as the electron microscope, which debuted in the 1950s, and the mapping of the human GENOME, completed in 2003 after 13 years of research, extended to the molecular level understanding of the seemingly simple yet incredibly intricate mechanisms that filter the blood and cleanse the body of metabolic wastes.

Breakthrough Research and Treatment Advances

The first successful KIDNEY TRANSPLANTATION in 1954, in which surgeons removed one healthy kidney from a man and transplanted it into his identical twin brother whose kidneys had completely failed, marked the advent of a new era in modern medicine. The discovery of cyclosporine, a powerful immunosuppressive DRUG, in 1954, made kidney transplantation a viable treatment for ESRD and paved the way for the transplantation of other vital organs such as livers and hearts. Today, surgeons in the United States perform more than 15,000 kidney transplantations each year, making the kidney the most frequently transplanted organ (aside from SKIN and corneas). Yet 45,000 people wait for donor kidneys. The shortage of donor kidneys has spurred efforts to find new solutions. One direction of research focuses on living kidney donation, in which a person agrees to provide one of his or her kidneys to a person whose own kidneys have failed. Advances in MINIMALLY INVASIVE SURGERY have significantly reduced the risks and inconveniences for living donors. Other directions of research focus on molecular medicine and genetics, looking for ways to correct problems with the kidneys to prevent kidney failure.

aging, urinary system changes that occur with At birth the structures of the urinary system are fully developed and function under the automatic control of the NERVOUS SYSTEM. The newborn's KIDNEYS filter BLOOD and make URINE. The BLADDER collects the urine and, when it fills to a point that triggers the micturition REFLEX, it empties to drain urine via the URETHRA to outside the body. Voluntary control over URINATION develops between three and five years of age, the rite of passage from babyhood to childhood. The urinary system typically then functions at a steady level for decades, unless disease alters its structures (notably the KIDNEYS).

Changes in the Kidneys and Bladder

Beginning around age 40 the number, size, and efficiency of nephrons, the filtering units of the kidneys, begins to diminish. At birth each kidney contains a million or more nephrons. By age 70 the kidneys have lost about 30 percent of the nephrons they contained at birth. They are smaller overall in size and take longer to filter the blood that flows through them. They may allow more water to enter the urine and keep more electrolytes in the blood circulation. The imbalance, even when slight, often affects BLOOD PRESSURE and other vital functions and increases the risk for DEHYDRATION.

Other changes in the body often affect the kidneys as well as other structures of the urinary system. With aging fibrous tissue throughout the body begins to lose elasticity, becoming more rigid. This reduced FLEXIBILITY can harden and narrow the blood vessels that supply the kidneys, slowing blood flow into the kidneys and through the nephrons. It also diminishes the bladder's ability to distend (expand), decreasing bladder capacity. Age-related changes in NERVE and BRAIN function also slow the micturition REFLEX, allowing the bladder to become more full before triggering the urge to urinate. These changes can result in URINARY URGENCY and URINARY FREQUENCY.

The Effects of Other Changes and Health Conditions

Age-related changes in the reproductive system—MENOPAUSE in women and BENIGN PROSTATIC HYPERPLASIA (BPH) in men—affect the urinary system as well. The normal and usually harmless enlargement with aging of the PROSTATE GLAND in men can constrict the urethra, interfering with the flow of urine during urination. Relaxation of the pelvic structures that accompanies the decline of the levels of ESTROGENS in women who are past menopause affects the woman's ability to control the flow of urine, allowing problems such as stress incontinence (urine leakage with coughing, sneezing, or laughing). As well, stretching and tearing of the pelvic muscles and ligaments that may have occurred during PREGNANCY and CHILDBIRTH may weaken these structures, allowing the bladder to sag and pressure the VAGINA (CYSTOCELE).

HYPERTENSION (high blood pressure) and DIABETES, two conditions that become increasingly common with advancing age, are particularly hazardous to the kidneys and between them account for about 80 percent of RENAL FAILURE (acute and chronic) and END-STAGE RENAL DISEASE (ESRD). Early and appropriate treatment for these conditions can significantly slow their actions on the kidneys, highlighting the importance of routine health screening for them. The risks for BLADDER CANCER, RENAL CANCER, NEPHROPATHY, NEPHROLITHIASIS (kidney stones), and UROLITHIASIS (bladder stones) also increase with age.

Measures to Maintain Urinary Health

Though it is not possible to prevent many of the health conditions affecting the urinary system that become more common with age, there are preventive lifestyle measures that can help maintain urinary health. These include

- drink a minimum of 8 to 12 eight-ounce glasses of water daily, more when it is hot or with exercise (urine should be colorless or slightly yellow)
- get blood pressure checked by a health-care provider at least yearly
- get checked for diabetes regularly
- urinate when the urge occurs and empty the bladder completely when urinating
- minimize use of over-the-counter products containing acetaminophen or NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)
- do not smoke (cigarette smoking accounts for 50 percent of bladder cancers)

Maintaining a healthy weight, nutritious EATING HABITS, and daily physical exercise are important for good health overall. People who have diagnosed hypertension or diabetes should strive to maintain the best possible control over these conditions through appropriate lifestyle measures and by taking medications as prescribed.

See also ATHEROSCLEROSIS; HEPATORENAL FAILURE; LIFESTYLE AND HEALTH; URINARY INCONTINENCE.

albuminuria Excessive excretion of ALBUMIN, a form of protein, into the URINE. Albuminuria, also called proteinuria, typically indicates kidney conditions that affect the glomeruli (the tubular structures within the KIDNEYS that filter wastes and excess water from the BLOOD to excrete in the urine). Such conditions include GLOMERULONEPHRITIS, GLOMERULOSCLEROSIS, NEPHROTIC SYNDROME, and NEPHROPATHY of DIABETES or of HYPERTENSION (high BLOOD PRESSURE). Albuminuria may accompany cardiovascular diseases such as ENDOCARDITIS and chronic inflammatory diseases such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) and RHEUMATOID ARTHRITIS. Strenuous physical exercise also can cause transient albuminuria without kidney disease.

Albuminuria does not itself cause symptoms. Most often the doctor detects albuminuria through urinalysis done during a ROUTINE MEDICAL EXAMINATION. Treatment targets the underlying cause. In the circumstance of chronic kidney disease, monitoring the urine albumin level is one method for assessing the status of kidney function. The urologist may conduct further diagnostic procedures such as ULTRASOUND or kidney biopsy when the cause of the albuminuria is undetermined. Persistent albuminuria typically suggests progressive damage to the kidneys regardless of the underlying cause.

See also AMYLOIDOSIS; MINIMAL CHANGE DISEASE.

Alport's syndrome An inherited genetic disorder in which one, two, or three mutations occur in the GENE that encodes type IV collagen formations, also called basement membranes. The mutations affect up to three of the six protein chains (alpha-3, alpha-4, and alpha-5) that make up type IV collagen, which is a foundation for a number of structures in the body including the glomeruli in the KIDNEYS, COCHLEA in the inner EAR, LENS of the EYE, and alveoli in the LUNGS. Among the three variations of Alport's syndrome, two include damage to these other structures as well as to the kidneys. All variations of Alport's syndrome include kidney damage that manifests as chronic GLOMERULONEPHRITIS (INFLAMMATION of the glomeruli), resulting in progressive scarring and fibrosis of the glomeruli. The fibrotic tissue replaces healthy tissue, preventing normal glomerular function.

The most common inheritance pattern for Alport's syndrome is X-linked, which affects about 80 percent of those who have the disorder. The syndrome may also occur as an autosomal recessive pattern (15 percent) or an autosomal dominant pattern (5 percent). All types of Alport's syndrome eventually progress to END-STAGE RENAL DISEASE (ESRD) in nearly everyone who has the disorder, though the rate of progression is highly variable and differs among the three inheritance patterns for the syndrome.

Symptoms and Diagnostic Path

The most common symptom of Alport's syndrome is HEMATURIA (bloody URINE) that may appear in

early childhood, typically following an upper respiratory viral INFECTION such as a cold. As the damage to the kidneys progresses, symptoms expand to include ALBUMINURIA (excessive albumin or protein in the urine) and HYPERTENSION (high BLOOD PRESSURE). About 80 percent of those who have Alport's syndrome develop neurosensory HEARING LOSS by ADOLESCENCE, and 15 percent have irregularities in the shape of the lens of the eye (lenticonus).

Symptoms in combination with family history strongly suggest Alport's syndrome, though kidney biopsy is the definitive diagnostic tool. Kidney biopsy, in which the urologist extracts a core of kidney tissue using a large-gauge needle, allows the him or her to determine the absence of any of the three affected protein chains as well as to assess the degree of damage already present. SKIN biopsy can confirm X-linked Alport's syndrome because the skin in this type of the disorder lacks the alpha-5 protein chain.

Treatment Options and Outlook

Treatment is primarily supportive and targets symptoms such as hypertension, hearing loss, and VISION IMPAIRMENT. For people who reach ESRD, KIDNEY TRANSPLANTATION often offers a viable therapeutic course. With treatment, many people who have Alport's syndrome are able to enjoy the lifestyles of their choosing well into the fifth or sixth decade of life. The likelihood of RENAL FAILURE increases with age, however.

Risk Factors and Preventive Measures

Because Alport's syndrome is an inherited genetic disorder, the only risks for this condition are the causative gene mutations. There are no measures to prevent the condition. Early treatment for consequential health conditions and close medical monitoring of kidney function help maintain optimal health.

See also ALVEOLUS; GENETIC DISORDERS; GLOMERULUS; INHERITANCE PATTERNS; MUTATION; RENAL DIALYSIS.

anuria The failure to produce URINE. Numerous circumstances can result in anuria, from severe DEHYDRATION and severe HYPOTENSION (low BLOOD PRESSURE) to END-STAGE RENAL DISEASE (ESRD) and RENAL FAILURE. Anuria requires prompt medical evaluation to determine and remedy the underlying cause. Without such correction, waste byproducts accumulate to toxic levels and the body cannot continue to function.

See also DYSURIA; ENURESIS; NOCTURIA; OLIGURIA; URINARY INCONTINENCE.

azotemia See UREMIA.

B

bladder A muscular, saclike structure in the lower pelvis that serves as a reservoir for the URINE the KIDNEYS produce. In women the bladder is in front of and slightly below the UTERUS. During PREGNANCY the expanding uterus limits the bladder's ability to expand, accounting for the URINARY FREQUENCY common in pregnancy's last trimester. In men the bladder is in front of the RECTUM, with the PROSTATE GLAND encircling the first segment of the URETHRA as it exits the bladder. Swelling of the prostate gland, such as typically occurs with advancing age, as in BENIGN PROSTATIC HYPERPLASIA (BPH), can constrict the flow of urine through the urethra in a man, accounting for symptoms such as urinary frequency and dribbling.

Three layers of tissue form the bladder. The outermost and innermost layers are membranous, the outer being a continuation of the peritoneum that lines the abdominal cavity and the inner being mucous-secreting epithelium. The bladder's middle layer is smooth MUSCLE called the detrusor muscle that itself has three layers, the fibers of each running differently. The outer muscle fibers run longitudinally (lengthwise), the middle muscle fibers form patterns of circles that ultimately culminate in the sphincter muscle that encloses the bladder's neck, and the inner muscle fibers run laterally (crosswise). Together these muscle layers allow the bladder to expand to accommodate the urine draining from the kidneys and also to contract, in coordination with relaxation of the urethral sphincter, to expel urine from the bladder through the urethra.

The ureters drain urine from the kidneys into the bladder; the urethra drains urine from the bladder to the outside of the body. One URETER, a narrow tubelike structure, drops from each kidney and enters the back wall of the bladder near its midline. Urine drips continuously from the ureters into the bladder. The urethra, a somewhat muscular tube, carries urine from the bladder to outside the body. When empty the bladder is about the size of a large lemon; when filled to its capacity of about 500 milliliters (32 to 34 ounces) the bladder can reach the size of a small cantaloupe. As the bladder expands it extends upward into the abdominal cavity.

URINATION, the process of expelling urine from the bladder (also called micturition), is an involuntary function that becomes an action of learned control. NEURON sensors in the muscle fibers of the bladder wall send NERVE signals to the sacral portion of the SPINAL CORD. This activates the micturition REFLEX, which sends nerve signals via the spinal cord to micturition centers in the BRAIN. These centers activate nerve impulses that cause the urethral sphincter to relax and the detrusor muscle to begin a series of wavelike contractions. These involuntary actions create the urge to urinate, experienced as a sensation of pressure.

Learning to control the pubococcygeal muscle, which forms the floor of the pelvis, serves to override the micturition reflex for a period of time. Relaxing the pubococcygeal muscle and contracting the abdominal muscles synchronize with the involuntary responses of the micturition reflex, and urination occurs. Most children acquire the developmental ability, a blend of conscious effort and neuromuscular maturity, to learn to control urination (commonly called bladder control) between the ages of three and five. With advanced age this control may diminish, a consequence of a weakened urethral sphincter, neurologic conditions, and other factors.

For further discussion of the bladder within the context of the urinary system's structure and

function please see the overview section "The Urinary System."

HEALTH CONDITIONS THAT CAN AFFECT THE BLADDER	
BLADDER CANCER	BLADDER EXSTROPHY
CYSTINURIA	CYSTITIS
CYSTOCELE	NEUROGENIC BLADDER
pyelonephritis	SPINA BIFIDA
URINARY INCONTINENCE	URINARY RETENTION
URINARY TRACT INFECTION (UTI)	URINARY URGENCY
UROLITHIASIS	VESICOURETERAL REFLUX

See also AGING, URINARY SYSTEM CHANGES THAT OCCUR WITH; BLADDER CATHETERIZATION; CYSTOSCOPY; FECAL INCONTINENCE; KEGEL EXERCISES.

bladder cancer The growth of a malignant (cancerous) tumor in the BLADDER. Bladder CANCER may be primary or metastatic (travel to the bladder from a point of origin elsewhere in the body). Doctors diagnose bladder cancer in about 55,000 Americans each year. Bladder cancer is about three times more common in men, and in the United States is the fourth most common cancer among men. Bladder cancer claims about 12,000 lives in the United States each year. The likelihood of developing bladder cancer increases with age.

Cigarette smoking causes about 50 percent of bladder cancers, and exposure to industrial chemicals accounts for another 25 to 30 percent. Among the chemicals known to cause bladder cancer are the aromatic amines: aniline, benzidine, chlornaphazine, methylene dianiline, naphthylamine, and xenylamine. Numerous industries use these chemicals. Tobacco smoke, too, contains aromatic amines.

There are several types of bladder cancers though in the United States one type, transitional-cell CARCINOMA (TCC), accounts for more than 90 percent of bladder cancers. TCC arises from the epithelial (also called urothelial) cells that form the innermost layer of the bladder's structure and typically undergo a series of predictable cell structure changes before becoming malignant. Other types of bladder cancer are relatively rare and include squamous cell carcinoma, small-cell carcinoma, LYMPHOMA, ADENOCARCINOMA, leiomyosarcoma, and metastatic malignant melanoma. Treatment options and outlook differ among the types of cancer.

Symptoms and Diagnostic Path

Painless HEMATURIA (bloody URINE) is often the earliest indication of bladder cancer. The hematuria may be gross, meaning there is enough BLOOD present to discolor the URINE, or microscopic, detected through urinalysis. Symptoms and signs of bladder cancer may include

- pink, red, or dark brown urine (hematuria)
- DYSURIA (discomfort when urinating)
- URINARY FREQUENCY
- URINARY URGENCY
- sensation of incomplete emptying of the bladder with URINATION

The diagnostic path begins with a standard urinalysis as well as specific urine tests to measure antigens and proteins present in the urine with TCC. These tests include

- NMP22 BladderChek, which detects the presence of nuclear matrix protein (NMP) 22
- BTA-Stat, which detects the presence of bladder tumor antigen (BTA)
- fibrin degradation products (FDPs), which detects the breakdown of blood clots

Further diagnostic procedures include CYSTOSCOPY, INTRAVENOUS PYELOGRAM (IVP), or COMPUTED TOMOGRAPHY (CT) SCAN to visualize the bladder and urethra to detect tumors, and biopsy (which the urologist typically does during cystoscopy) of identified tumors or suspicious tissue. Biopsy provides the conclusive diagnosis, allowing the pathologist to identify the type of cancer and degree to which it has spread (staging and grading).

Treatment Options and Outlook

The cancer's type and stage determine treatment options and outlook. Doctors diagnose about 70 percent of TCC in its early stages, when the tumor is small and remains confined to a localized region of the epithelium. These tumors, designated as superficial or stage 0, are highly treatable with minimally invasive therapies that generally preserve the bladder and normal urinary functions. These therapies may include

STAGING OF BLADDER CANCER (TCC)

Stage	Extent of Cancer	Treatment Protocols/Options
0	cancer cells are in a single localized area in the the superficial cells of the urothelium (epithelial cells that form the lining of the BLADDER) also called carcinoma in situ (CIS)	one or a combination of • transurethral resection (TUR) with fulguration (cystoscopic removal of the tumor and electrocautery to the adjacent tissue) • intravesical BCG (bacillus Calmette-Guérin instilled into the bladder via urethral catheter) • intravesical chemotherapy (chemotherapy instilled into the bladder via urethral catheter) • photodynamic therapy
1	tumor remains confined to the urothelium	TUR with fulguration *or* segmental cystectomy (partial removal of the bladder) in combination with one or more adjunctive therapies: • intravesical BCG • intravesical CHEMOTHERAPY • radioactive seeding (implantation of radioactive pellets) • systemic chemotherapy
2	tumor extends into but not beyond the detrusor MUSCLE	radical cystectomy (removal of bladder and surrounding organs and tissues in combination with one or more adjunctive therapies: • RADIATION THERAPY • radioactive seeding • chemotherapy urinary diversion (urostomy, reservoir)
3	tumor extends beyond the bladder wall to surrounding tissue tumor may invade the PROSTATE GLAND (men) or CERVIX, UTERUS, VAGINA, or OVARIES (women)	preoperative chemotherapy radical cystectomy (including removal of lymph nodes and any other organs to which the cancer has spread) urinary diversion postoperative radiation therapy, chemotherapy, or both
4	tumor extends into the structures of the pelvis and abdomen tumor may extend into adjacent lymph nodes metastatic cancer may appear in sites distant from the bladder	preoperative chemotherapy radical cystectomy (including removal of lymph nodes and any other organs or structures to which the cancer has spread) urinary diversion postoperative chemotherapy, radiation therapy, or both alternatively, palliative radiation therapy to shrink the tumors and relieve symptoms
Recurrent	tumor comes back after treatment tumor may recur in the bladder or appear elsewhere in the urinary tract or distant from the bladder	surgery, chemotherapy, radiation therapy or a combination, depending on the cancer's location and previous treatments

- transurethral resection (TUR) with fulguration, a bladder-sparing treatment in which the urologist removes the tumor via cystoscopy and uses electrocautery to burn an area of surrounding tissue to kill any stray cancer cells
- intravesical BCC, in which the urologist instills a solution of bacillus Calmette-Guérin (BCC) to stimulate an IMMUNE RESPONSE that targets any residual cancer cells or isolated cancer cells elsewhere in the urothelium
- intravesical CHEMOTHERAPY, in which the urologist instills chemotherapy drugs into the bladder to target residual cancer cells topically
- photodynamic therapy, in which the person takes a chemical the cancer cells absorb that makes them extraordinarily sensitive to certain frequencies of light

Cancer that spreads into the urothelium or beyond requires more aggressive treatment, typically surgery to remove the tumor and surrounding tissue in combination with chemotherapy, RADIATION THERAPY, or both, and sometimes other therapies such as photodynamic therapy and intravesical BCC. In a segmental cystectomy the urologist removes part of the bladder; in a radical cystectomy the urologist removes all the bladder along with adjacent structures and organs, depending on the extent of the cancer. Segmental cystectomy usually preserves enough of the bladder to retain function and urinary continence.

Radical cystectomy requires further surgery to construct URINARY DIVERSION such as a urostomy, which drains urine continuously into a bag worn attached to the outside of the body, or an internal pouch structured from a loop of intestine that collects urine. With the pouch method, the urologist may be able to fashion a reservoir that collects the urine from the kidneys, and attach it to the urethra for normal continence and urination. When this is not possible or practical, the urologist may be able to construct an opening (stoma) into which the person inserts a catheter to regularly drain urine that collects in the reservoir.

Many of the treatment options for bladder cancer entail significant lifestyle changes. Radical cystectomy and radiation therapy often result in ERECTILE DYSFUNCTION in men, inability to have vaginal intercourse in women, and sterility in men and women. It is important to fully understand the potential side effects, complications, and QUALITY OF LIFE implications of the various treatment options when making treatment decisions and to obtain a second opinion consultation. Research is ongoing for new therapies, and some people may benefit from participating in clinical trials.

Risk Factors and Preventive Measures

Bladder cancer is very rare in people under age 40. Cigarette smoking and occupational exposure to aromatic amines are the leading causes of bladder cancer, and health experts believe both to be preventable. It appears the highest risk of bladder cancer associated with cigarette smoking is for people who have smoked for several decades. The risk for bladder cancer appears to remain elevated even after stopping smoking. Some health experts believe current and former smokers should have annual urinalysis and urine cytology tests such as NMP22 BladderChek beginning at age 60.

Though exposure-related bladder cancer takes years to decades to develop, researchers believe even brief, limited exposure to aromatic amines may be sufficient to cause damage to the cells of the bladder that later results in bladder cancer. Most people who develop exposure-related bladder cancer have had long-term exposure to aromatic amines, however. Exposure-related bladder cancer generally develops over 15 to 20 years from the time of exposure, though can emerge up to 40 or 50 years later. Strict federal regulations limiting occupational exposure to known carcinogens such as aromatic amines have reduced risk somewhat over the past several decades, though the use of these chemicals remains so pervasive across numerous industries that exposure remains second only to cigarette smoking as a risk factor for bladder cancer.

OCCUPATIONS WITH HIGH AROMATIC AMINES EXPOSURE

chemical manufacturing	hairdresser
leatherworker	machinist
metalworker	painter
printer	rubber manufacturing
textile worker	

Certain treatments for other cancer may raise the risk for bladder cancer. These include radiation therapy to the pelvic region, notably women who received such treatment for ENDOMETRIAL CANCER or CERVICAL CANCER or men for PROSTATE CANCER, and chemotherapy with cyclophosphamide or ifosfamide. People who have had such treatments should receive ROUTINE MEDICAL EXAMINATION with urinalysis and diagnostic procedures as doctor recommended for early detection of bladder cancer.

See also CANCER TREATMENT OPTIONS AND DECISIONS; LYMPH NODE; METASTASIS; SKIN CANCER; STAGING AND GRADING OF CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

bladder catheterization The insertion of a narrow, flexible tube into the BLADDER through the URETHRA to drain URINE from the body. Bladder catheterization may be necessary to collect an uncontaminated (sterile) urine sample or to drain urine from the bladder. The catheter placement may be short term, such as after surgery or during serious illness, or long term, such as when STROKE, PARALYSIS, or other condition results in loss of bladder control (complete URINARY INCONTINENCE).

Long-term catheterization may be intermittent, in which the caregiver periodically inserts the catheter to drain collected urine and then removes the catheter, or indwelling (often called a Foley catheter), in which the catheter remains tethered in the bladder (a small inflatable balloon at the tip of the catheter keeps the catheter from sliding out of the urethra). An indwelling catheter drains into a collection bag which the person or caregiver empties frequently and regularly. A caregiver must replace an indwelling catheter every four to six weeks for hygienic reasons. Many people who have indwelling catheters or who use long-term intermittent catheterization take ANTIBIOTIC PROPHYLAXIS to prevent URINARY TRACT INFECTION (UTI). Bladder catheterization greatly increases the risk for UTI. Proper hygiene is essential when inserting and removing a bladder catheter and when an indwelling catheter is in place.

See also CYSTITIS; SPINAL CORD INJURY; TRAUMATIC BRAIN INJURY (TBI).

bladder exstrophy An uncommon CONGENITAL ANOMALY in which the structures of the lower pelvis fail to form properly. As a consequence, the BLADDER protrudes outside the body and may be open or inverted. The URETHRA often fails to close as well. Bladder exstrophy is a random birth defect and is not a hereditary birth defect. About 100 infants are born with bladder exstrophy, which varies widely in severity, each year in the United States.

Treatment in most cases is surgery within several days of birth to reconstruct and reposition the bladder, urethra, symphysis pubis, and other pelvic structures. Most children born with bladder exstrophy require follow-up operations through early childhood and perhaps at PUBERTY when secondary sex characteristics alter the appearance and function of the GENITALIA. However, even with surgical repair or reconstruction the urethral sphincter muscle at the neck of the bladder may not function properly, resulting in incomplete control over the flow of URINE. This URINARY INCONTINENCE may remain throughout life, though there are medical therapies and lifestyle methods to manage the condition. VESICOURETERAL REFLUX, in which urine flows (refluxes) from the bladder back up the ureters, is also common.

Appropriate reconstructive surgery maintains FERTILITY. Men may experience RETROGRADE EJACULATION, in which SPERM travel inward through the urethra and into the bladder during ejaculation rather than outward through the urethra to exit the PENIS. In such a circumstance a fertility expert can retrieve the sperm and place them into the woman to achieve fertilization. Women born with bladder exstrophy generally are able to carry PREGNANCY to term and deliver vaginally as long as the circumstances of the pregnancy permit.

See also BIRTH DEFECTS; EPISPADIAS.

bladder stone See UROLITHIASIS.

C–D

cystinuria An inherited genetic disorder in which the KIDNEYS do not properly reabsorb amino acids collectively called cystine. The excessive excretion of cystine to the URINE causes crystalline calcifications, commonly called stones, to form in the kidneys, ureters, and BLADDER. Most people learn they have the GENE MUTATION, which is autosomal recessive, during analysis of the calcifications. Doctors have known of cystine calcifications in the bladder since the early 1800s. Researchers identified cystinuria as hereditary in the early 1900s and discovered the first effective medication to reduce the formation of cystine calcifications, penicillamine, in the early 1960s. In the late 1990s researchers identified the mutated genes as SLC3A1 on CHROMOSOME 2 and SLC7A9 on chromosome 19.

Pain in the side or back, often on only one side, is the typical symptom of an occlusive (blocking) calcification. The urine may also smell of sulfur (rotten eggs) The diagnostic path may include ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI) of the abdomen to visualize the calcifications. Laboratory analysis of fragments filtered from the urine identifies their composition as cystine, confirming the diagnosis. Most of the time the stones pass on their own, though the process often is painful. Doctors usually prescribe ANALGESIC MEDICATIONS for PAIN relief during the time a stone is passing. Occasionally treatments such as EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL), which uses high-frequency sound waves to break the calcification into fragments, or surgery (percutaneous nephrolithotomy) are necessary to remove an obstructive and impacted stone.

Because there are as yet no treatments to correct the gene mutation, the cystine calcifications recur throughout life. Penicillamine, which binds with cystine in the urine to form a compound that easily dissolves in water, remains the medication urologists most often prescribe to reduce the formation of stones. The urologist may also prescribe medications to increase the alkalinity of the urine, such as potassium citrate, which helps dissolve cystine. It is important for people who have cystinuria to drink enough water to maintain good urine output, which dilutes the concentration of cystine and pass it from the body before it forms calcifications. Other lifestyle modifications include decreasing dietary sodium and protein consumption (protein is the source of the cystine).

See also ENDOSCOPY; FANCONI'S SYNDROME; GENE THERAPY; HYPEROXALURIA; INHERITANCE PATTERNS; NEPHROLITHIASIS; SURGERY BENEFIT AND RISK ASSESSMENT; UROLITHIASIS.

cystitis INFLAMMATION of the BLADDER. The most common cause of cystitis is bacterial INFECTION, called URINARY TRACT INFECTION (UTI). Other pathogens, such as fungi (yeasts) and viruses, also can cause infectious cystitis. Nonpathogenic causes of cystitis include irritation of the lining of the bladder, which may occur with excessive consumption of irritating substances such as CAFFEINE, high-acid foods, or certain medications. Cigarette smoking is a significant bladder irritant. RADIATION THERAPY, CHEMOTHERAPY, and AUTOIMMUNE DISORDERS also may cause cystitis. Interstitial cystitis is a chronic condition the hallmark of which is inflammation of the bladder along with a constellation of symptoms for which there are no clearly identifiable causes.

Symptoms and Diagnostic Path

The symptoms of cystitis may include

- DYSURIA (burning or PAIN with URINATION)

- HEMATURIA (bloody URINE)
- URINARY URGENCY
- URINARY FREQUENCY, including NOCTURIA (the need to urinate at night)
- cloudy, foul-smelling, or discolored urine
- pain in the lower abdomen
- pain with SEXUAL INTERCOURSE

The diagnostic path begins with urinalysis, which often shows whether BACTERIA or other pathogens are present in the urine. *Escherichia coli* is the most commonly the culprit for infectious cystitis (UTI). *Chlamydia* and herpes simplex viruses (HSV-1 and HSV-2) are also common causes of UTIs. The urologist may choose further diagnostic procedures such as CYSTOSCOPY or abdominal ULTRASOUND to rule out causes such as tumors or stones (UROLITHIASIS). Cystoscopy allows the urologist to assess bladder capacity, an important factor in determining a diagnosis of interstitial cystitis as reduced bladder capacity is a characteristic of this condition. The current standard of diagnosis for interstitial cystitis further requires the presence of key symptoms over a period of time as well as the exclusion of other causes for the symptoms.

Treatment Options and Outlook

UTIs require therapy with the appropriate medications, such as ANTIBIOTIC MEDICATIONS for bacterial infections or ANTIFUNGAL MEDICATIONS for yeast-based infections. The symptoms of infectious cystitis generally subside within a few days of beginning treatment, and the infection clears with the full course of medication. The oral medication phenazopyridine (Pyridium) acts as a topical anesthetic to block pain signals from the lining of the bladder, easing dysuria until the medication affects the infection. It is essential to take prescribed medications as the doctor directs and to take medications to treat infections until the medication is gone (the full course of treatment) even after symptoms improve. Undertreated or untreated UTIs can migrate from the bladder to the KIDNEYS, where they can cause serious illness and sometimes permanent damage to the kidneys.

Treatment for autoimmune cystitis targets the IMMUNE SYSTEM with ANTIHISTAMINE MEDICATIONS, IMMUNOSUPPRESSIVE MEDICATIONS, and other approaches that aim to block the inflammatory response. Irritation cystitis often resolves with a combination of increased fluid consumption and ending the cause of the irritation, when possible. Common culprits include coffee, tea, carbonated beverages, citrus fruits and juices, tomatoes and tomato products, chocolate, ALCOHOL, and pickled or smoked foods.

Interstitial cystitis is difficult to treat. People respond differently to treatment regimens, and sometimes a successful treatment becomes ineffective. Urologists may prescribe various kinds of medications to relieve symptoms such as tricyclic ANTIDEPRESSANT MEDICATIONS (which appear to suppress certain pain response mechanisms), NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), and antihistamines. The medication pentosan (Elmiron) is the only oral medication specifically for interstitial cystitis, though women who are pregnant cannot take it. Pentosan also takes up to six months to provide relief and may cause temporary HAIR loss. Other treatments include intravesical therapies in which the urologist instills medications directly into the bladder via urethral catheterization. Bladder distention under ANESTHESIA (via cystoscopy) provides long-term though temporary relief for some people.

FOODS AND DRINKS THAT CAN IRRITATE THE BLADDER

beer	cantaloupe
chocolate	chocolate-covered espresso beans
coffee	cranberries and cranberry juice
cola beverages	onions
lemons and lemonade	peanuts and peanut butter
mixed ALCOHOLIC drinks	pineapple
oranges and orange juice	tomatoes and tomato juice
peppers (sweet or hot)	wine (white or red)
tea (hot or iced)	
vinegar and dressings with vinegar	

Risk Factors and Preventive Measures

Women are more likely to develop infectious cystitis and interstitial cystitis, primarily because a woman's shorter URETHRA allows easier access for pathogens. Diligent personal hygiene, including urination soon after sexual intercourse and wiping toilet tissue from front to back, helps reduce exposure to bacteria. Doctors are unsure why intersti-

tial cystitis occurs more often in women. However, doctors do not know what causes interstitial cystitis, either. Finding the cause will likely shed light on all dimensions of this chronic and disruptive condition.

See also BLADDER CATHETERIZATION; NEPHRITIS.

cystocele A hernialike condition in which a woman's BLADDER bulges into her VAGINA. Cystocele is more common after MENOPAUSE and in women who have given birth vaginally. It occurs as a consequence of weakened vaginal and pelvic muscles and ligaments that allow the supportive structures for the bladder to relax and the bladder itself to drop. Doctors believe the prime culprit is the intense straining that occurs during vaginal birth, which weakens muscles, coupled with changes in the elasticity of MUSCLE tissue that take place when levels of ESTROGENS drop in a woman's body with menopause.

The symptoms of cystocele may include the sensation of vaginal pressure, difficulty urinating, or URINARY RETENTION. Chronic URINARY TRACT INFECTION (UTI) may also occur, especially when the extent of the cystocele is such that residual URINE remains in the bladder after URINATION. The doctor can usually diagnose cystocele via vaginal palpation during a PELVIC EXAMINATION, as the sagging bladder causes the vaginal wall to bulge inward. When the diagnosis or the extent of the cystocele is uncertain the doctor may conduct a voiding CYSTOURETHROGRAM to determine whether the bladder fully empties with urination.

Mild cystocele that causes no symptoms may require only watchful waiting. The urologist or gynecologist may also recommend a pessary, a device placed within the vagina that gives added support to the vaginal wall. Surgical repair is the treatment of choice for cystocele that interferes with urination, particularly when such interference causes chronic UTI. The surgery tightens the ligaments and muscles of the pelvic floor, restoring support for the bladder. Open surgery requires six to eight weeks for full recovery. Often the surgeon can do the repair laparoscopically, reducing recovery time to two to three weeks.

See also HYDROCELE; KEGEL EXERCISES; MINIMALLY INVASIVE SURGERY; RECTOCELE; SPERMATOCELE; SURGERY BENEFIT AND RISK ASSESSMENT; VARICOCELE.

cystoscopy An endoscopic procedure for visualizing the interior of the BLADDER. The cystoscope is a narrow tube with a tiny light and camera on the tip. Cystoscopy requires no preparation or recovery time and takes place in an outpatient surgery setting under sterile procedures. The urologist anesthetizes the URETHRA, then inserts the cystoscope through the urethra and into the bladder, visualizing the progress on a closed-circuit television monitor. Some people find the insertion mildly uncomfortable. The urologist then injects saline through the cystoscope to fill the bladder, which may create the urge to urinate. However, the bladder must be full to distend its walls for complete examination. Cystoscopy takes 10 to 20 minutes.

Cystoscopy allows the urologist to visualize the interior of the bladder to examine it for signs of INFLAMMATION or tumors (BLADDER CANCER). The urologist can use cystoscopy to biopsy suspicious findings, remove bladder stones, and administer medications such as antibiotics or anti-inflammatory drugs. Cystoscopy also allows the urologist to evaluate BENIGN PROSTATIC HYPERPLASIA (BPH) in men. Some people experience HEMATURIA (BLOOD in the urine) and discomfort or burning (DYSURIA) with URINATION for a day or two after cystoscopy, a consequence of the cystoscope irritating the urethral tissues. The urologist should evaluate dysuria or hematuria that continues beyond two days as this may indicate a URINARY TRACT INFECTION (UTI) requiring ANTIBIOTIC MEDICATIONS; the cystoscope may carry BACTERIA from the SKIN's surface into the urethra and bladder.

See also ENDOSCOPY; UROLITHIASIS.

cystourethrogram A diagnostic imaging procedure that shows the flow of URINE from the BLADDER through the URETHRA. The radiologist instills a radio-opaque solution (contrast medium) into the bladder through a catheter, then takes a series of X-rays as the solution fills the bladder and urethra. The radio-opaque solution makes these soft tissue structures visible on X-RAY. In a voiding cystourethrogram, the radiologist takes additional X-rays with the person urinating, to visualize the entire flow of urine.

Cystourethrogram shows structural abnormalities, such as narrowing or stricture, of the urethra

and functional problems, such as VESICOURETERAL REFLUX (a condition in which urine flows back into the ureters from the bladder). The procedure requires no preparation or recovery and takes about 20 minutes to complete. Some people experience discomfort during the instillation of the contrast medium because it creates the pressure of a full bladder. Minor discomfort or burning may occur with URINATION for a day or two after the procedure.

See also BENIGN PROSTATIC HYPERPLASIA (BPH); BLADDER CATHETERIZATION; CYSTOSCOPY; URETER; URETHRAL STRICTURE.

dialysis See RENAL DIALYSIS.

dysuria PAIN, discomfort, or burning with URINATION. Dysuria may be primarily external (occur with the passing of URINE through the URETHRA) or internal (felt as discomfort, pressure, or pain within the lower pelvis). Dysuria is most commonly a symptom of CYSTITIS (INFLAMMATION or INFECTION of the BLADDER and urethra), though it occurs as a symptom of numerous conditions involving the genitourinary tract. The diagnostic path begins with urinalysis and may include other diagnostic procedures, depending on the full spectrum of symptoms and the findings of the urinalysis. Treatment targets the identified causative condition.

CONDITIONS FOR WHICH DYSURIA IS A COMMON SYMPTOM

BENIGN PROSTATIC HYPERPLASIA (BPH)	CHLAMYDIA
CYSTITIS	EPIDIDYMITIS
GONORRHEA	NEUROGENIC BLADDER
PELVIC INFLAMMATORY DISEASE (PID)	PROSTATITIS
pyelonephritis	sexual trauma
TRICHOMONIASIS	URETHRITIS
URINARY TRACT INFECTION (UTI)	UROLITHIASIS
VAGINITIS	

See also ANURIA; ENURESIS; HEMATURIA; NOCTURIA; OLIGURIA; URINARY INCONTINENCE; UROLITHIASIS.

end-stage renal disease (ESRD) A condition of permanent RENAL FAILURE in which the KIDNEYS can no longer function to filter wastes from the BLOOD. People who have ESRD require ongoing RENAL DIALYSIS and may be appropriate candidates for KIDNEY TRANSPLANTATION. DIABETES, HYPERTENSION (high BLOOD PRESSURE), and GLOMERULONEPHRITIS are the most common causes of ESRD in the United States. About 300,000 Americans live with ESRD, about 15,000 of whom undergo kidney transplantation each year. ESRD typically follows a period of chronic renal failure that extends for years to several decades. More than 40 percent of Americans who have ESRD are between the ages of 45 to 64.

About a third of people who have ESRD survive five years on renal dialysis, whereas 80 to 90 percent who receive transplanted kidneys live five years after the transplant operation, the five-year marker being a key assessment point for the success of treatment. The waiting list for a cadaver donor kidney (a kidney donated after a person's death) varies widely because donors and recipients must match, and it can be two or three years before one receives a kidney because the supply of donor organs is so limited. An increasingly popular option is living donor transplantation, in which a person (often a family member) who provides a close match for BLOOD TYPE and blood antigens and has two healthy kidneys donates one kidney for transplantation into the person who has ESRD. Each year in the United States nearly 80,000 people die from ESRD.

The U.S. federal government's health-care program for older Americans, Medicare, extends coverage to those of any age who have ESRD. Medicare covers many though not all the costs of renal dialysis and kidney transplantation. Private health insurance and state-funded programs may provide further benefits for those who qualify.

See also MEDICARE COVERAGE FOR PERMANENT RENAL FAILURE; ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

enuresis An inability to hold the URINE, particularly at night (nocturnal enuresis). A common term for enuresis is bedwetting. Enuresis is primarily a condition of childhood though may persist into adulthood, depending on the cause and treatment efforts. About 85 percent of children are developmentally mature enough to master voluntary control of the bladder sphincter between the ages of 3 and 6. Generally enuresis that persists beyond the age of 12 is either secondary to other physical conditions or psychological in origin. Enuresis is more common among boys.

Conditions commonly associated with enuresis include CYSTITIS, NEUROGENIC BLADDER, and urethral obstruction such as CONGENITAL ANOMALY or obstructive calcifications. Occasionally the cause is damage to the lower SPINAL CORD or to the SPINAL NERVES that control BLADDER function. In teens or adults who develop enuresis, the enuresis may be an early sign of DIABETES or indicate other health conditions such as OBSTRUCTIVE SLEEP APNEA (which disrupts the body's normal sleep rhythms), SEIZURE DISORDERS, or HYPERTHYROIDISM (overactive THYROID GLAND). Obstructive sleep apnea may also be a factor in children between the ages of two and five who have enlarged adenoids, which is a common circumstance among this age group, that block the back of the throat when lying down. Research in the late 1990s suggests some people who have enuresis experience dysfunction of the neurologic interactions that regulate the depth of sleep and initiate sleep arousal.

In some children the causes of enuresis are primarily behavioral, such as ignoring the urge to urinate until it becomes overwhelming, not emptying the bladder immediately before going to bed, or drinking large quantities of fluids throughout the day and especially in the three to four hours preceding bedtime. Generally these behaviors are easy for parents to modify through positive reinforcement and diligent monitoring of the child's drinking and URINATION patterns. Psychological enuresis typically occurs due to profound emotional distress and is not the result of conscious behavior.

Enuresis becomes a significant embarrassment to most who have it after they reach about the age of 8 to 10 and especially for teens and adults. Children may refuse to spend the night with friends or have friends spend the night with them and may avoid overnight activities such as camping or vacationing in motels. Their refusal may be overt or they may express unreasonable fears.

Symptoms and Diagnostic Path

The symptom of enuresis is inappropriate urination, often during naps or when sleeping at night, but it may occur any time. The diagnostic path consists of a careful history of eating, drinking, urination, and bowel habits as well as patterns of enuresis (such as all the time or only during sleep). The urologist may conduct diagnostic procedures such as urinalysis, ULTRASOUND of the bladder, voiding CYSTOURETHROGRAM, or CYSTOSCOPY, depending on the suspected underlying cause. In most situations in which the urinalysis is normal, however, the urologist delays extensive diagnostic procedures until after a trial of basic treatment and behavioral interventions.

Treatment Options and Outlook

Treatment may combine medical interventions with behavioral approaches such as limiting fluids in the evening and fully emptying the bladder right before going to bed. Enuresis alarms (moisture-sensitive devices) are especially effective for children. Medication therapy may include desmopressin (DDAVP), which decreases urine production, or oxybutynin (Ditropan) or tolterodine (Detrol), medications that slow smooth muscle stimulation.

Risk Factors and Preventive Measures

Nocturnal enuresis appears to run in some families, though researchers are not sure what accounts for this. The key risk factors for enuresis are organic causes such as congenital anomalies or physiologic dysfunctions and severe emotional stress. Health experts stress that neither punishment nor the so-called bladder training method (holding a full bladder for a determined amount of time, ostensibly to strengthen sphincter control) is effective in ending enuresis. These approaches fail to address the causes of enuresis, result in further embarrassment and discomfort, and may exacerbate the underlying cause of the enuresis. Time, patience, and positive reinforcement (such as praise and small rewards) as well as appropriately addressing any physiologic dysfunctions, result in ending enuresis about 98 percent of people.

See also ANURIA; CONGENITAL ANOMALY; DYSURIA; HEMATURIA; NEURAL TUBE DEFECTS; NOCTURIA; OLIGURIA; SLEEP DISORDERS; URINARY INCONTINENCE; URINARY URGENCY.

epispadias A random CONGENITAL ANOMALY in which the URETHRA forms incorrectly. Epispadias often occurs as an element within a constellation of congenital malformations involving the pelvic structures (including the pelvic bones) and the GENITALIA.

In boys the urethra may exit the PENIS other than at the tip or appear as an open channel that runs the length of the PENIS, and often occurs in conjunction with CHORDEE (a deformity in which the penis curves sharply). In girls the urethra may exit anywhere between the neck of the BLADDER and the upper labial fold, and typically occurs in conjunction with genital deformities such as bifid (two-fold or split) CLITORIS and abnormalities of the VULVA.

Epispadias is rare in either sex though much more so in girls, and typically apparent at birth. Early surgery is the preferred means to correct the defects, which preserves FERTILITY and sexual function, restores the genitalia to normal appearance, and helps establish urinary continence (the ability to control the flow of URINE). Prenatal ULTRASOUND sometimes can detect epispadias before birth. There are no measures to prevent epispadias.

See also BIRTH DEFECTS; BLADDER EXSTROPHY; HYPOSPADIAS; PRENATAL CARE.

extracorporeal shock wave lithotripsy (ESWL) A therapeutic procedure in which a machine called a lithotriptor generates shock waves that cause calcifications within the urinary tract, commonly called kidney stones (NEPHROLITHIASIS) or bladder stones (UROLITHIASIS), to break apart into smaller fragments the URINE can carry out of the body. Lithotripsy became available in 1980 and has evolved into the current treatment of choice for stones smaller than 2 centimeters (about 0.75 inch) in diameter that form in the KIDNEYS, URETER, and BLADDER. ESWL is sometimes effective for gallstones (cholelithiasis) as well. Today there are several types of lithotriptors, each of which uses a different energy source though all apply the same basic approach which is to focus a pulse of intense energy (the shock wave) at the stone.

Women who are or could be pregnant should not undergo ESWL.

Typically preparation requires having nothing to eat or drink for six hours before the scheduled time of the procedure. The urologist or nephrologist may recommend stopping routine use of NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), aspirin, and anticoagulation medications for 7 to 10 days before the scheduled ESWL to reduce the risk of bleeding during or after the procedure, as these medications interfere with PLATELET AGGREGATION and prolong the length of time a BLOOD clot takes to form. ESWL takes about an hour to perform, with about two hours in the recovery room afterward. The person undergoing ESWL treatment will need someone to take him or her to and from the treatment center.

Procedure

The urologist or radiologist generally gives the person an anesthetic or sedative for comfort before the ESWL begins. The pressure of the shock waves coming in contact with the stones can be uncomfortable. The lithotriptor integrates FLUOROSCOPY or ULTRASOUND to pinpoint the location of the targeted stone and can target several stones in one ESWL session. The person wears a hospital gown and lies on a cushioned table. The ESWL technician positions the lithotriptor over the person to deliver the shock waves, with continual monitoring and adjustment to maintain accurate focus. The radiologist or urologist makes sure the person has adequate ANESTHESIA or SEDATION to remain comfortable for the duration of the procedure.

Risks and Complications

The most common risk associated with ESWL is bleeding from the tissues around the site of the stone, resulting in HEMATURIA (bloody urine) and some discomfort. Many people experience discomfort for up to several days after the ESWL, for which the urologist prescribes ANALGESIC MEDICATIONS (pain relief). Most people should plan on taking it easy for a few days after ESWL. It may take days to weeks for all of the fragments to pass, and larger fragments may cause pain when they pass. Sometimes fragments of the stone cluster in the ureter or URETHRA, temporarily blocking the flow of urine and causing considerable PAIN. Generally movement (such as walking) and drinking lots of fluids help flush these clusters from the body, with appropriate analgesic medication to mitigate the pain. Some people require several ESWL sessions to completely disperse all of the stones and fragments.

Outlook and Lifestyle Modifications

Once the stone breaks apart and the fragments pass from the body in the urine, no further treatment for the stone is necessary. The urologist or nephrologist may recommend dietary changes, increased physical activity, increased water consumption, and sometimes medications to help prevent new stones from forming. Such factors depend on the stone's content and the person's medical history, including other health conditions. Both kidney stones and bladder stones tend to recur.

See also CYSTINURIA; GALLBLADDER DISEASE; SURGERY BENEFIT AND RISK ASSESSMENT.

Fanconi's syndrome A dysfunction of the KIDNEYS in which the renal tubules do not function properly, resulting in a constellation of diverse symptoms. The renal tubule, a structure of the kidney's filtering mechanism within the NEPHRON, filters many substances from the BLOOD to retain those the body needs and excrete those the body

does not need. In Fanconi's syndrome, the renal tubule excretes into the URINE numerous vital substances it should retain in the blood. Among these substances are GLUCOSE, uric acid, calcium, magnesium, potassium, phosphate, and amino acids. The renal tubule also excretes excessive water into the urine.

Numerous GENETIC DISORDERS cause Fanconi's syndrome. Among the most common are metabolic conditions that affect the body's ability to use or store substances such as cystine, glycogen, fructose, and tyrosine. HEAVY-METAL POISONING, such as from lead or mercury, and DRUG toxicity account for most acquired Fanconi's syndrome. Conditions such as AMYLOIDOSIS, in which protein deposits accumulate in organs such as the kidneys, also can damage the renal tubules to cause Fanconi's syndrome. The syndrome occasionally develops in people who undergo KIDNEY TRANSPLANTATION.

Equally numerous symptoms can suggest Fanconi's syndrome and may appear initially to be unrelated. In children the most common symptoms are stunted growth, BONE deformities similar to those which occur in RICKETS, and MUSCLE weakness. In adults, the most common symptoms are spontaneous FRACTURE, electrolyte imbalance, and serum acidosis (increased acidity of the blood). General symptoms sometimes present in children or adults include excessive thirst and URINATION, CONSTIPATION, and DEHYDRATION. Blood and urine tests identify the depletions and excesses of the substances the renal tubules are failing to reabsorb.

Treatment targets the underlying cause when doctors can identify it and the resulting conditions when the underlying cause remains unknown (idiopathic Fanconi's syndrome). Doctors can treat many genetic disorders of METABOLISM from early childhood, forestalling or preventing complications such as Fanconi's syndrome. With appropriate treatment kidney function can return to normal. Untreated Fanconi's syndrome can progress to END-STAGE RENAL DISEASE (ESRD), requiring long-term RENAL DIALYSIS or kidney transplantation.

See also CYSTINURIA; ENVIRONMENTAL HAZARD EXPOSURE; MINERALS AND HEALTH; OSTEOPOROSIS; WILSON'S DISEASE.

glomerulonephritis INFLAMMATION of the glomeruli within the nephrons of the KIDNEYS. The glomerulus is the coiled capillary network through which BLOOD circulates for filtration. Glomerulonephritis, also called glomerular disease, may be acute (come on suddenly) or chronic (develop slowly over time). Acute glomerulonephritis is often a temporary condition that improves with treatment and causes minimal or no residual damage to the glomeruli. Chronic glomerulonephritis tends to be progressive, eventually deteriorating to RENAL FAILURE and END-STAGE RENAL DISEASE (ESRD). INFECTION, AUTOIMMUNE DISORDERS, NEPHROPATHY of DIABETES, and nephropathy of HYPERTENSION (high BLOOD PRESSURE) are the most common identified causes of glomerulonephritis. As often as not, however, the nephrologist cannot determine the cause and focuses instead on treatment.

Symptoms and Diagnostic Path

The symptoms of glomerulonephritis may be minimal and difficult to detect or obvious and debilitating, depending on whether the condition is chronic or acute. Common symptoms of glomerulonephritis include

- fatigue
- edema (swelling or puffiness) of the face, hands and wrists, and feet and ankles
- discolored URINE (commonly described as tea-colored or cola-colored)
- hypertension
- foamy urine (ALBUMINURIA)

The diagnostic path begins with urinalysis, which typically reveals HEMATURIA (blood in the urine) and albuminuria (excessive ALBUMIN, or protein, in the urine). In many people, urinalysis done as part of a ROUTINE MEDICAL EXAMINATION provides the first indication of glomerulonephritis. Blood tests help the nephrologist assess the ability of the kidneys to remove toxins and wastes from the blood. Imaging procedures such as abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN can show the damage to the glomeruli. Needle biopsy of the kidney tissue allows microscopic examination of the glomeruli, providing the definitive diagnosis.

Treatment Options and Outlook

Treatment targets either the underlying condition or the resulting symptoms. Because hypertension is nearly always either a cause or a consequence of glomerulonephritis, the doctor is likely to prescribe medications that lower blood pressure (antihypertensives) such as beta blockers, angiotensin-converting enzyme (ACE) inhibitors, or calcium channel blockers. The doctor may also prescribe medications to extract more water from the blood (diuretics), which lowers blood pressure as well as eases the workload of the kidneys. Bacterial infections require ANTIBIOTIC MEDICATIONS. Viral infections, which are fairly common, will run their course after which kidney function usually returns to normal.

Acute glomerulonephritis may result in renal failure, requiring short-term RENAL DIALYSIS to remove wastes and toxins from the blood until kidney function returns enough to resume this functions. CORTICOSTEROID MEDICATIONS and other immunosuppressive therapies are necessary when the cause of the glomerulonephritis is an autoimmune disorder. Once the cause of the inflammation resolves, the glomerulonephritis generally resolves as well, and kidney function returns to normal.

Chronic glomerulonephritis may require long-term medication therapy, and presents a significant risk for progression to ESRD despite treatment.

Risk Factors and Preventive Measures

Diabetes and hypertension are the leading risk factors for glomerulonephritis. Keeping these conditions under control with medications and lifestyle methods lowers the likelihood for damage to the kidneys and can slow the progression of chronic glomerulonephritis. Untreated or undertreated (failing to complete the full course of antibiotics) strep infections such as STREP THROAT or IMPETIGO remain a significant source of bacterial infection that causes glomerulonephritis. Though there are no methods for preventing glomerulonephritis, the doctor may recommend measures to slow its progression such as dietary modifications (less sodium, potassium, and protein; more water consumption).

See also GOODPASTURE'S SYNDROME; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; NEPHRITIS; NEPHRON; NEPHROTIC SYNDROME; POLYARTERITIS; SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).

glomerulosclerosis The formation of SCAR tissue (fibrosis) within the glomeruli, the coiled capillary networks within the nephrons of the KIDNEYS. The most common presentation of glomerulosclerosis is focal segmental glomerulosclerosis in which the fibrosis is scattered throughout the glomeruli, affecting only parts of the GLOMERULUS in various nephrons. The damage permanently blocks the affected glomeruli, however. Because the kidneys have millions of nephrons, glomerulosclerosis may be under way for a significant time before it causes enough damage to manifest symptoms. Some forms of glomerulosclerosis are familial (have a hereditary component) and others arise in conjunction with INFECTION such as HIV/AIDS. Most often, however, the glomerulosclerosis is idiopathic—the nephrologist can find no cause for the scarring. Though some researchers believe the cause is autoimmune, glomerulosclerosis does not respond to IMMUNOSUPPRESSIVE THERAPY.

Symptoms and Diagnostic Path

Early symptoms of glomerulosclerosis are vague and may not appear to be symptoms at all. They include

- poor APPETITE in combination with weight gain
- edema (swelling) of the face, hands and wrists, and feet and ankles
- foamy URINE, indicating ALBUMINURIA (excretion of ALBUMIN, a form of protein, in the urine)
- discolored urine, indicating HEMATURIA (BLOOD in the urine)

The diagnostic path begins with urinalysis, which typically reveals the albuminuria as well as hematuria. Needle biopsy of the kidney shows the fibrosis among the glomeruli and may also show the presence of immunoglobulins characteristic of the condition. HYPERTENSION (high BLOOD PRESSURE) is also often present, a consequence of damage that affects the parts of the NEPHRON that produce a key HORMONE essential for blood pressure regulation (RENIN). Because the kidneys also produce ERYTHROPOIETIN (EPO), the hormone that stimulates the BONE MARROW to produce erythrocytes (red blood cells). Erythrocytes carry oxygen in the blood circulation. Progressive glomerulosclerosis often results also in ANEMIA (insufficient oxygen in the blood circulation).

Treatment Options and Outlook

There is no cure for glomerulosclerosis, which in most people progresses over about 10 years to END-STAGE RENAL DISEASE (ESRD). Treatment includes medications to control blood pressure. As CHOLESTEROL BLOOD LEVELS also tend to be high (HYPERLIPIDEMIA), the doctor may prescribe medications and lifestyle changes to help bring them down. These therapies may slow the progression of the fibrosis. The progressive loss of protein further damages the nephrons. At the point of ESRD, long-term RENAL DIALYSIS or KIDNEY TRANSPLANTATION is necessary to sustain life.

Risk Factors and Preventive Measures

Glomerulosclerosis, particularly focal segmental, tends to develop in people who are in their 20s and 30s and is about three times more common among African American males. There are no measures to prevent glomerulosclerosis. Managing the symptoms as effectively as possible may delay the onset of ESRD. Kidney transplantation becomes the treatment option that offers the greatest opportunity for a return to normal activities.

See also GLOMERULONEPHRITIS; MEDICARE COVERAGE FOR PERMANENT RENAL FAILURE; NEPHROTIC SYNDROME.

glomerulus The coiled capillary network within the NEPHRON of the kidney through which BLOOD passes for filtration. Glomeruli are abundant within the KIDNEYS as each kidney contains more than a million nephrons. The walls of the glomerulus are only a few cells in thickness. The glomerular walls are semipermeable, allowing smaller molecules such as water, metabolic wastes, GLUCOSE, and electrolytes to pass through and collect in the capsule (called Bowman's capsule) that surrounds the glomerulus. Together the glomerulus and Bowman's capsule are the renal corpuscle. The fluid and its contents, called filtrate, passes into the tubules of the nephron, which further filter and concentrate the filtrate. The nephron eventually reabsorbs 99 percent of the filtrate back into the blood; the remaining fluid drains into collecting ducts to move out of the kidneys as URINE. The glomerular filtration rate (GFR) is an important measure of kidney function. The GFR of a healthy adult kidney is 125 milliliters per minute.

For further discussion of the glomerulus within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also GLOMERULONEPHRITIS; GLOMERULOSCLEROSIS; RENAL FAILURE.

Goodpasture's syndrome An autoimmune disorder in which the IMMUNE SYSTEM produces antibodies that attack the glomeruli in the KIDNEYS, impairing kidney function, and the alveoli in the LUNGS, causing bleeding into the lung tissue. In most people who develop Goodpasture's syndrome the symptoms follow a viral INFECTION of the upper respiratory tract or exposure to environmental toxins, notably hydrocarbons. Because Goodpasture's syndrome tends to run in families, researchers believe a GENE MUTATION is likely responsible.

Siphoning gasoline and sniffing aerosols such as paints and glues are the most common exposures to hydrocarbons that can result in Goodpasture's syndrome.

Though the coughing up of bloody SPUTUM (HEMOPTYSIS) is the first and often the more distressing sign of Goodpasture's syndrome, GLOMERULONEPHRITIS is the more serious consequence, leading rapidly in many people to RENAL FAILURE. ANEMIA (insufficient erythrocytes in the blood) and HYPERTENSION (elevated BLOOD PRESSURE), consequences of the renal failure, may quickly become significant.

SYMPTOMS OF GOODPASTURE'S SYNDROME

Pulmonary (Lungs)	Renal (Kidneys)
HEMOPTYSIS (bloody SPUTUM)	HEMATURIA (bloody URINE)
DYSPNEA (shortness of breath)	foamy urine (indicates ALBUMINURIA)
COUGH	decreased urine volume
CHEST PAIN	edema (fluid retention)

The diagnostic path includes blood and urine tests to assess kidney function, chest X-RAY to detect accumulated fluid in the lungs, and biopsy of lung and kidney tissue to confirm the presence of antibodies. The course of Goodpasture's syndrome may run two months to several years. Early diagnosis allows aggressive interventions, including plasmapheresis to remove antibodies from the bloodstream and IMMUNOSUPPRESSIVE THERAPY to prevent the immune system from producing further antibodies. These interventions can mediate the syndrome's progression, minimizing damage to the kidneys. Though about 90 percent of those who develop this once-fatal syndrome now survive, many of them continue to experience progressive renal failure that results in END-STAGE RENAL DISEASE (ESRD).

See also ALVEOLUS; ANTIBODY; AUTOIMMUNE DISORDERS; HEMAPHERESIS; GLOMERULUS; RENIN.

H

hematuria BLOOD in the URINE. Hematuria may result from numerous circumstances and always requires medical evaluation to determine the underlying cause. Though BLADDER CANCER is uncommon, hematuria often is the earliest sign of its presence. Gross hematuria occurs when the amount of blood in the urine is sufficient to discolor the urine (typically pink, red, or brown). Occult, or microscopic, hematuria occurs when the amount of blood in the urine is very slight, detected during microscopic examination of the urine.

Urinalysis is the first step of the diagnostic path, with additional diagnostic procedures, depending on the findings and the symptoms. Treatment targets the underlying cause. Certain medications or foods may cause the urine to be pink or red, in which case the urinalysis shows there to be few erythrocytes (red blood cells) present in the urine. MENSTRUATION may also give the appearance of blood in the urine.

CONDITIONS FOR WHICH HEMATURIA IS A COMMON SYMPTOM

BENIGN PROSTATIC HYPERPLASIA (BPH)	BLADDER CANCER
BLUNT TRAUMA to the abdomen or back	CHLAMYDIA
CYSTITIS	EPIDIDYMITIS
GENITAL TRAUMA	GONORRHEA
PROSTATITIS	pyelonephritis
TRICHOMONIASIS	URETHRITIS
URINARY TRACT INFECTION (UTI)	UROLITHIASIS

See also ANURIA; DYSURIA; ENURESIS; NOCTURIA; OLIGURIA.

hemolytic uremic syndrome RENAL FAILURE that occurs as a rare complication in children after INFECTION with *Escherichia coli* O157:H7 acquired from contaminated food. *E. coli* O157:H7 causes hemorrhagic ENTERITIS, itself a life-threatening infection. Hemolytic uremic syndrome occurs when the toxins the *E. coli* O157:H7 release enter the bloodstream. The toxins destroy erythrocytes (red BLOOD cells) and platelets (clotting cells). Remnants of the destroyed blood cells clog the glomeruli within the KIDNEYS, preventing blood from flowing through these filtering structures. As more glomeruli become affected, the kidneys can no longer filter toxins from the blood.

Symptoms and Diagnostic Path

The symptoms of hemolytic uremic syndrome begin to emerge as the child appears to be recovering from the enteritis. The earliest indication of hemolytic uremic syndrome is the appearance of PETECCHIAE, pinpoint hemorrhages under the surface of the SKIN, in a child recovering from *E. coli* O157:H7 hemorrhagic enteritis. Other symptoms include reduced URINE volume, fatigue, irritability, and pale skin. Blood tests typically show the damaged blood cells and indications of diminishing kidney function. However, the child becomes life-threateningly ill very rapidly, requiring immediate hospitalization and intensive medical treatment.

Treatment Options and Outlook

There is no cure for hemolytic uremic syndrome. Treatment consists of intensive supportive care while the condition runs its course, including efforts to maintain the child's fluid and electrolyte balances as well as RENAL DIALYSIS to filter toxins from the blood. The renal failure disrupts all body systems and functions, often causing severe HYPERTENSION (high BLOOD PRESSURE), other cardiovascular problems, LIVER dysfunction, and neurologic dysfunction. With prompt and aggressive medical

care, 80 percent of children survive. About 70 percent of them recover fully with no residual health problems. Among the other 30 percent renal failure progresses to END-STAGE RENAL DISEASE (ESRD), often within months though sometimes over several years, requiring long-term renal dialysis and ultimately KIDNEY TRANSPLANTATION.

Risk Factors and Preventive Measures

Hemolytic uremic syndrome is a rare complication of *E. coli* O157:H7 hemorrhagic enteritis, so any child who acquires this infection incurs the risk for the syndrome. There are no measures to prevent hemolytic uremic syndrome as a complication of *E. coli* O157:H7 infection. Even with prompt and aggressive medical care for the hemorrhagic enteritis, hemolytic uremic syndrome remains a potential complication. The most effective preventive measures are precautions to protect against *E. coli* O157:H7 infection. Such measures include

- wash hands with hot, soapy water before and after handling meats
- do not handle other foods when preparing meats
- use separate, nonporous surfaces and utensils (not wooden) to prepare meats for cooking
- wash food preparation surfaces and utensils with hot soapy water immediately after preparing meats
- thoroughly cook all meats to the recommended temperatures for the kind of meat
- thoroughly rinse all fruits and vegetables in cold running water before eating or preparing them

See also FOOD-BORNE ILLNESSES; GLOMERULUS.

hepatorenal failure The progressive failure of the KIDNEYS in people who have chronic LIVER FAILURE. Doctors do not know what causes hepatorenal failure, also called hepatorenal syndrome, to develop though they do know the BLOOD supply to the kidneys becomes suddenly and severely restricted. Not enough blood flows through the kidneys for the kidneys to filter waste byproducts and toxins from the blood, and these substances accumulate in the blood. Because the kidneys play key roles in regulating BLOOD PRESSURE, HYPERTENSION (elevated blood pressure) may also develop.

The primary symptom of hepatorenal failure is diminished URINE production in a person who has chronic liver failure. Symptoms of liver failure are also often present and typically include ASCITES (fluid retention in the abdominal cavity), JAUNDICE (yellowish discoloration of the skin), and abnormal bleeding. Blood and urine tests help evaluate liver and kidney function, and diagnostic imaging procedures such as abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN demonstrate the extent of physical damage to the liver and the kidneys.

Treatment aims to improve both liver and kidney functions. RENAL DIALYSIS often becomes necessary. In some people the kidneys remain healthy and return to full function when the underlying liver disease improves, such as might occur with LIVER TRANSPLANTATION. When liver disease is severe, however, the progressive failure of the kidneys means the body loses nearly all of its ability to remove toxins and the risk of death is very high.

See also CIRRHOSIS; COAGULATION; ENCEPHALOPATHY; LIVER DISEASE OF ALCOHOLISM.

horseshoe kidney A random CONGENITAL ANOMALY in which a band of tissue fuses the KIDNEYS at the bottom, forming a shape resembling a horseshoe. The tissue band, called an isthmus, may be fibrous or the same tissue as the kidneys. In most people who have this anomaly, both kidneys are fully functional. However, the fusion distorts the normal structure of the kidneys, leading over time to conditions such as HYDRONEPHROSIS (dilation of the renal pelvis), NEPHROLITHIASIS (kidney stones), and VESICOURETERAL REFLUX (backflow of URINE from the BLADDER into the ureters and kidneys). The BLOOD vessels that supply the horseshoe kidney are often intertwined and anomalous, providing abnormal blood flow to the fused kidney that can affect its functions. The horseshoe kidney also resides lower in the abdominal cavity, placing it outside the protective enclosure of the rib cage. Horseshoe kidney increases the risk for some types of primary RENAL CANCER.

Two thirds of people who have horseshoe kidney learn of the anomaly during diagnostic proce-

dures for other health concerns. Doctors diagnose most others in the course of identifying the causes for conditions that affect the kidneys. When symptoms do occur, they generally represent a consequential condition such as nephrolithiasis. The diagnostic path includes blood and urine tests to assess kidney function. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or renal ULTRASOUND can provide visual evidence of the fused kidneys. Diagnostic prenatal ultrasound often detects horseshoe kidney in the unborn child.

For the most part horseshoe kidney of itself presents no unusual health risks. The fused kidneys are prone to the same conditions that affect kidneys in general. Treatment targets any conditions affecting the kidney. The urologist or nephrologist may suggest surgery (nephroplasty) to separate the kidneys and establish normal positioning of the ureters and the blood supply. Watchful waiting, with routine medical care to monitor kidney function and health, is appropriate for many people who have no symptoms of kidney disease. Researchers do not know what causes horseshoe kidney to occur. One child born with horseshoe kidney does not increase the likelihood that other children will also have the anomaly; the condition appears to be entirely random.

See also EPISPADIAS; HYPOSPADIAS; TURNER'S SYNDROME.

hydronephrosis A circumstance in which the renal pelvis, the portion of the kidney that collects URINE for passage from the kidney via the URETER, dilates and enlarges. Hydronephrosis results from conditions of the kidney that slow or block the flow of urine, causing urine to back up into or pool in the renal pelvis. Such conditions may include obstructive NEPHROLITHIASIS (kidney stones that block the ureter), NEUROGENIC BLADDER (in which the BLADDER fails to respond to the normal neurosensory signals that regulate URINATION and becomes overly full), and VESICOURETERAL REFLUX (urine washes back into the ureters from the bladder).

Unilateral hydronephrosis, which affects only one kidney, is the more common presentation. Bilateral hydronephrosis, which affects both KIDNEYS, often indicates CONGENITAL ANOMALY of kidney or ureteral structure though may develop as a consequence of conditions such as HYPERTENSION (high BLOOD PRESSURE), DIABETES and BENIGN PROSTATIC HYPERPLASIA (BPH) that constricts the urethra and slows the flow of urine during urination.

The symptoms of hydronephrosis may include

- abdominal or back PAIN
- DYSURIA (discomfort or burning with urination)
- URINARY FREQUENCY
- URINARY URGENCY
- signs of INFECTION such as FEVER and cloudy or bloody urine

Some people may have no symptoms, with the hydronephrosis showing up during evaluation of other medical concerns or in PREGNANCY. The diagnostic path begins with urinalysis and blood tests to evaluate kidney function and usually includes an abdominal X-RAY, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, INTRAVENOUS PYELOGRAM (IVP), or MAGNETIC RESONANCE IMAGING (MRI) examination to visualize the kidneys. Treatment targets the underlying disease process to restore the free flow of urine. Untreated hydronephrosis results in permanent damage to the kidney that may lead to RENAL FAILURE.

See also HEMATURIA; HORSESHOE KIDNEY; NEPHRITIS; NOCTURIA; URINARY TRACT INFECTION (UTI).

hypercalciuria Excessive excretion of calcium in the URINE. About 80 percent of people who have kidney stones (NEPHROLITHIASIS) or BLADDER stones (UROLITHIASIS) have hypercalciuria. In most people the circumstance appears a combination of factors that typically include high dietary calcium intake, insufficient water consumption (resulting in low urine volume), and physical inactivity. The water and citrate content of the urine normally allows most of the calcium the KIDNEYS extract from the BLOOD to dissolve and pass from the body. When urine volume and citrate concentration are low, calcium in the urine combines with other minerals (usually oxalate or phosphate) to form crystalline structures. Over time these structures harden or calcify (called calculi). Inactivity contributes to calculus formation because it allows mineral sediments to settle, facilitating their crystallization.

Other causes of hypercalciuria include endocrine disorders such as HYPERPARATHYROIDISM and ADDISON'S DISEASE, kidney dysfunction, and MALABSORPTION disorders of the gastrointestinal system. Many people who have hypercalciuria do not have nephrolithiasis or urolithiasis, though the presence of excess calcium in the urine raises their risk for developing either condition. Routine urinalysis often detects hypercalciuria. Doctors generally recommend increased water consumption, maintaining dietary calcium intake at recommended levels for BONE health, and daily physical activity. Many people also benefit from thiazide diuretic medications, which act to slow the extraction of calcium in the kidneys as well as to increase the volume of urine. Many stones that form as a consequence of hypercalciuria will pass through the urinary tract without medical intervention, though they require treatment when they cause significant pain or an obstruction in the kidney, URETER, bladder, or URETHRA.

See also CYSTINURIA; FANCONI'S SYNDROME; HYPEROXALURIA; RENAL TUBULAR ACIDOSIS.

hyperoxaluria Excessive OXALATE excretion in the URINE. Oxalate is a natural chemical that enters the body through dietary sources such as vegetables, fruits, and grains. The LIVER also metabolizes oxalate. Researchers do not know what benefits the body derives from oxalate. However, in the body oxalate attracts calcium, creating the insoluble compound calcium oxalate. About 80 percent of kidney stones are made of calcium oxalate. Deposits of calcium oxalate may also accumulate in tissues such as the KIDNEYS, liver, HEART, and bones, a circumstance known clinically as oxalosis.

Most hyperoxaluria is idiopathic (without a clearly identifiable cause). Doctors believe about 50 percent of people who have mild to moderate hyperoxaluria consume an abundance of foods high in dietary oxalate. In some people the binding between calcium and oxalate intensifies for reasons researchers do not understand though believe results from genetic factors. Less commonly, hyperoxaluria occurs as an autosomal recessive genetic disorder that results in the absence of an enzyme the body requires to break down oxalate into soluble components that are more easily excreted. Genetic hyperoxaluria generally causes symptoms (typically kidney or bladder stones) in early childhood. Rarely, hyperoxaluria is a secondary complication of MALABSORPTION disorders, such as SHORT BOWEL SYNDROME and INFLAMMATORY BOWEL DISEASE (IBD), that alter the gastrointestinal tract's absorption of dietary calcium and oxalate.

The most common symptoms are kidney stones (NEPHROLITHIASIS) or bladder stones (UROLITHIASIS). The diagnostic path includes laboratory tests to measure the levels of oxalate in the urine and the BLOOD, analysis of any stones, and family history. Dietary modifications (eating fewer foods with high oxalate content) are often treatment enough for mild idiopathic hyperoxaluria. Other therapeutic approaches include medications to increase the ability of the urine to dissolve calcium and oxalate salts, magnesium and pyridoxine (vitamin B_6) supplementation, and increasing water consumption to dilute the urine. Primary (genetic) hyperoxaluria typically results in RENAL FAILURE by early adulthood with the only definitive treatment being KIDNEY TRANSPLANTATION.

See also ADDISON'S DISEASE; HYPERCALCIURIA; HYPERPARATHYROIDISM; ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

hypospadias A CONGENITAL ANOMALY in which the URETHRA is shorter than normal and exits along the underside of the PENIS in a boy or into the VAGINA in a girl. Though uncommon overall, hypospadias is very rare in girls. In boys, CHORDEE (severely curved penis) often accompanies hypospadias. The preferred treatment is surgery to extend the urethra to its normal length and path. In boys, such surgery also includes correction of the chordee. The surgery establishes normal URINATION and, in boys, restores structural integrity to the penis that will permit sexual function and FERTILITY later in life. The urologist typically performs the OPERATION when the child is between 6 and 12 months of age. More than 90 percent of such corrective surgery produces a functionally and cosmetically acceptable repair. Some children may need more than one operation, notably boys in whom the urethral opening is near the base of the penis.

See also BIRTH DEFECTS; BLADDER EXSTROPHY; EPISPADIAS.

interstitial cystitis See CYSTITIS.

intravenous pyelogram (IVP) A diagnostic imaging procedure to evaluate the flow of BLOOD and URINE through the KIDNEYS, ureters, BLADDER, and URETHRA. IVP requires moderate preparation that typically includes taking a laxative the night before the scheduled procedure to empty the intestines so the IVP provides clear visualization of the renal structures and then consuming nothing by mouth until after the IVP. An IVP takes about an hour to complete though does not require any recovery time after the procedure.

A radiologist performs IVP by injecting an iodine-based contrast medium into a VEIN in the arm. Some people experience a mild burning sensation with the contrast medium's injection. The person lies on the X-RAY table, and the radiologist takes X-rays at timed intervals as the contrast medium travels through the bloodstream and into the kidneys.

Sometimes the radiologist uses an inflatable compression belt, applied around the abdomen and back, to slow progress of the contrast medium through the kidneys. Near the end of the procedure the person urinates to empty the bladder, after which the radiologist takes a final series of X-rays.

It is important to drink plenty of water after an IVP to help flush the residual contrast medium from the body. Complications and side effects are rare, the most common being an allergic reaction to the contrast medium. People who have allergies to iodine or shellfish should discuss the possibility of sensitivity to the contrast medium with the radiologist or urologist before undergoing the IVP. The IVP provides an abundance of information about the structure and functions of the urinary system that is useful for the urologist in reaching or confirming diagnosis of numerous conditions affecting the kidneys.

See also COMPUTED TOMOGRAPHY (CT) SCAN; CYSTOURETHROGRAM.

K

Kegel exercises A series of exercises to strengthen the pubococcygeal muscle, a figure-eight double loop of MUSCLE that forms the pelvic floor. Arnold H. Kegel, MD, an American gynecologist who practiced in Los Angeles, California, popularized the pelvic muscle exercises that now bear his name when he developed a BIOFEEDBACK device called a perineometer in the 1940s. Though urologists and gynecologists had been instructing women in the procedure of these exercises for over a decade as treatment for URINARY INCONTINENCE, most women had no idea whether they were doing them correctly. The Kegel perineometer was the first device to measure the effectiveness of the cycles of contraction and relaxation of the pubococcygeal muscle. In conjunction with biofeedback, Kegel exercises became highly successful in resolving mild to moderate urinary incontinence in many women.

PERFORMING KEGEL EXERCISES

- Identify the pubococcygeal muscle by stopping and starting the flow of URINATION or, for women, inserting a finger into the VAGINA. Women or men may benefit from BIOFEEDBACK methods.
- Begin with 10 repetitions of the complete cycle of contract, hold, and relax. Maintain each stage for 10 seconds. Repeat three times a day.
- As pubococcygeal muscle STRENGTH improves, increase the length of each stage to 20 seconds and the number of repetitions gradually to 50. Repeat three times a day.

Kegel exercises, also called pelvic floor exercises, today remain the most effective noninvasive treatment for urinary incontinence in women—and in men after surgery to treat BENIGN PROSTATIC HYPERPLASIA (BPH) or PROSTATE CANCER. Many obstetricians recommend Kegel exercises to speed recovery after CHILDBIRTH. Kegel exercises are also often helpful for treating premature EJACULATION in men. The exercises are very simple, consisting of cycles of contracting, holding, and relaxing the pubococcygeal muscle repeated several times a day. Once a person learns the exercises, he or she can perform them unnoticeably and when seated, standing, or lying down.

It is important to correctly identify the pubococcygeal muscle; the muscles of the buttocks, abdomen, and thighs should be relaxed when performing Kegel exercises. An easy way to learn to contract the pubococcygeal muscle is to consciously stop and start the flow of URINE when urinating. BIOFEEDBACK remains the most effective means for determining whether the person is performing the Kegel exercises correctly, and a variety of biofeedback devices are available for home use. Women may also use a simple device called a vaginal cone. Most people begin to experience results in about six to eight weeks. It is important to continue regularly with Kegel exercises to maintain optimal pubococcygeal muscle tone and STRENGTH.

See also FECAL INCONTINENCE.

kidney cancer See RENAL CANCER.

kidney cyst See RENAL CYST.

kidney dialysis See RENAL DIALYSIS.

kidney disease of diabetes See NEPHROPATHY.

kidney donor An individual who donates his or her KIDNEYS after death or who donates one kidney

for live donor transplantation. Kidneys are the organs most commonly transplanted in the United States (other than SKIN and corneas). At present, people waiting for donor kidneys outnumber available kidneys nearly four to one. Between 50,000 and 60,000 people currently await donor kidneys in the United States. A person becomes a potential candidate for KIDNEY TRANSPLANTATION with the onset of END-STAGE RENAL DISEASE (ESRD), a permanent state of renal failure in which the kidneys cannot perform their functions at a level that sustains life.

The donor and the recipient must match in BLOOD TYPE and human leukocyte antigen factors and be negative for antibodies (negative crossmatch). HUMAN LEUKOCYTE ANTIGENS (HLAS) are six inherited proteins (three from each parent) on the surfaces of leukocytes (white BLOOD cells). The more HLAs that match, the greater likelihood the recipient's body will accept the donor kidney. Even with blood type match and good HLA matching, some people's immune systems produce antibodies in reaction to the donor's blood. A negative crossmatch mixes small amounts of the prospective donor's blood and the recipient's blood to confirm that there is no ANTIBODY reaction.

Living Donor

A living donor may be a relative or a stranger to the kidney recipient. In general a living donor must be in overall good health and have two normally functioning kidneys. Some health conditions, such as HYPERTENSION (high BLOOD PRESSURE), chronic LIVER disease, and DIABETES, preclude a person from donating a kidney because the risk is high for developing kidney disease as a consequence of these conditions. People with chronic health conditions generally are not eligible to donate a kidney. There is no greater likelihood of developing kidney disease with only one kidney, and a single kidney can more than adequately accommodate the body's needs.

The transplant team selects a living donor on the basis of the match between the donor and the recipient. Typically, the recipient's health insurance pays for the donor's medical expenses related to the kidney donation, including surgery, hospitalization, and follow-up care. Once selected, the living donor undergoes NEPHRECTOMY, an OPERATION to remove a kidney. There are two options, open nephrectomy and laparoscopic nephrectomy. Either procedure is a major surgery that requires hospitalization and postsurgical recovery time. Though recovery is uneventful for most donors whether they undergo laparoscopic or open nephrectomy, donating a kidney does require time off from work and regular activities.

Laparoscopic nephrectomy requires several small incisions through which the team uses laparoscopy to remove the donor kidney. Though technically more challenging for the transplant team, laparoscopic nephrectomy significantly reduces scarring and recovery time for the donor. Laparoscopic nephrectomy takes three to four hours, with two to three hours in the recovery room while the person returns to full consciousness. Most people who undergo laparoscopic nephrectomy stay one to three days in the hospital after the surgery and require four to six weeks for return to regular activities. Within a year or two, the small scars remaining from the incisions are nearly invisible.

Open nephrectomy requires a single large incision and takes two to three hours, with two to three hours in the recovery room to return to full consciousness. Most people who undergo open nephrectomy stay three to five days in the hospital after the surgery and need six to eight weeks for return to regular activities. The SCAR from the incision begins to fade in about a year.

The transplant team immediately performs the transplantation surgery to place the donor kidney into the recipient. Only the intended recipient may receive the living donor kidney; there are no waiting list requirements for live donor kidney transplantations. Living donor kidney transplants have a higher long-term success rate than cadaver donor kidney transplants.

Cadaver Donor

Cadaver donor kidneys come from the bodies of deceased persons who died of causes not related to kidney function, had healthy kidneys at the time of death, and signed documents affirming their desires to donate their organs after their deaths. Family members may make the decision about organ donation when the person dies without organ donor documentation. Organ donation can

proceed only when the appropriate assessments certify the person has suffered BRAIN DEATH.

UNIVERSAL DONOR CARD

Most states honor the universal donor card, a wallet-size document affirming a person's intent to donate his or her organs upon death, as a legal document. Many states incorporate the universal donor card into the driver's license.

A transplant team removes donor kidneys using sterile surgical technique and a procedure similar to nephrectomy (surgical removal of a kidney such as to treat RENAL CANCER), carefully preserving the blood vessels and URETER. After removing the kidneys, called organ harvesting, the transplant team places them in a cold solution that can sustain them for 36 to 48 hours and sutures closed the incisions made to gain access to the kidneys. The organ-processing procedure includes screening of the donor kidneys for any diseases they could convey to the recipient. In the United States an independent organization called the United Network for Organ Sharing (UNOS) oversees the collection and distribution of all cadaver donor organs in compliance with strict guidelines intended to ensure equity in the process of matching donor organs with recipients. The transplant surgery must take place within 36 to 48 hours of the kidney's harvesting, sooner if possible.

See also ORGAN TRANSPLANTATION; QUALITY OF LIFE; SURGERY BENEFIT AND RISK ASSESSMENT.

kidney failure See RENAL FAILURE.

kidneys A pair of organs responsible for filtering wastes and excess water from the BLOOD, excreting both from the body as URINE. The kidneys maintain the body's fluid and electrolyte balances, and also produce hormones that regulate the production of new erythrocytes (ERYTHROPOIETIN [EPO]) and BLOOD PRESSURE (RENIN). With each heartbeat about 20 percent of the body's blood supply surges through the kidneys. The body's entire blood supply passes through the kidneys about two dozen times a day. Though the kidneys are essential for life, a single functioning kidney can adequately sustain life in most people. The kidneys are fully functional from birth.

Renal Structure

The kidneys are dark reddish brown in color, four to five inches long, and about two inches across. An adult kidney weighs five to six ounces, and is the same shape as the bean that bears its name. The kidneys rest against along the spinal column at the back of the abdominal cavity, one on each side of the SPINAL CORD and within the protective enclosure of the rib cage. The kidneys are retroperitoneal—that is, they lie outside the posterior layer of the peritoneum, the membrane that protects the abdominal structures. The left kidney is about an inch higher than the right. A cushion of fatty tissue surrounds each kidney, helping protect it as well as hold it in place. An adrenal gland resides atop each kidney though does not physically or functionally integrate with the kidney.

A thin but tough membrane called the renal capsule surrounds the kidney, helping contain and protect its blood-rich tissues. The outer layer of the kidney is the renal cortex and the inner layer the renal medulla. The renal ARTERY, renal VEIN, and URETER junction with the kidney where it indents, an area called the hilus. Deeper within the kidney at this junction is the renal pelvis, a deltalike region of the kidney that drains urine into the ureter. The functional unit of the kidney is the NEPHRON, a microscopic structure, a set of tubules that carry out the functions filtration, and a coil of capillaries, the GLOMERULUS, which brings in the blood for filtration. Each kidney contains over a million nephrons, each of which functions independently. The nephrons extend through the renal cortex and the renal medulla. The renal cortex contains the blood vessels that bring blood to the nephrons and the glomerulus for each nephron, as well as a portion of filtering tubule. The renal medulla consists of 8 to 12 wedge-shaped segments, called pyramids. The pyramids contain the filtering tubules, including the loop of Henle and the collecting tubule, for each nephron. Blood circulates primarily through the renal cortex, while the structures of the renal medulla direct water and waste products (urine) toward the renal pelvis and elimination via the ureter.

Renal Function

The pressure of the blood as it flows through the glomeruli helps force molecules of water and

other substances across the membranous glomerular walls and into an encapsulated structure called Bowman's capsule. Specialized proteins called transporters carry these substances across the capillary membranes. The collected mixture, called filtrate, funnels from the Bowman's capsule into the tubules. A separate capillary network, the peritubular capillaries, entwines the filtration tubules to allow water and other substances to return to the blood circulation (reabsorption). By the time a heartbeat's surge of blood completes its passage through the nephrons, about 99 percent of the water and electrolytes originally filtered from the blood (sodium, potassium, magnesium, calcium, and others) have returned to the circulation.

Kidney function remains at a fairly constant level for much of life. By the 40s, the kidneys begin to lose nephrons at a rate of about 10 percent per decade. As a single kidney can meet the body's needs having only about one third of its capacity, the kidneys are well structured to function the length of the lifespan. The primary threats to kidney function are diseases that affect other body systems or the body as a whole, such as DIABETES, HYPERTENSION (high blood pressure), and CARDIOVASCULAR DISEASE (CVD).

The kidneys also produce two vital hormones: RENIN, which controls blood pressure, and EPO, which regulates erythropoiesis (the synthesis of new erythrocytes in the BONE MARROW). Health conditions that damage the kidneys also affect their ability to produce these hormones. Interstitial cells (cells in the body of the kidney) produce both hormones.

The pressure of blood flowing through the glomeruli helps determine whether the kidney releases renin, which is a process of perpetual balance. Renin sets in motion the cascade of events through which the body produces angiotensin II, a potent vasoconstrictor (chemical that narrows and stiffens the blood vessels to raise blood pressure). The kidneys also respond to the release of ANTIDIURETIC HORMONE (ADH) from the HYPOTHALAMUS, another mechanism of blood pressure regulation that influences the amount of water the kidneys withhold in the blood or excrete in the urine. The hypothalamus releases ADH to cause the kidneys to withhold more water, which increases the blood volume and thus the blood pressure.

The kidneys also detect the level of erythrocytes that are in the blood as it passes through them, and release erythropoietin when the erythrocyte level drops. Erythropoietin stimulates the production of reticulocytes in the bone marrow and their release into the blood circulation, where they mature to become oxygen-bearing erythrocytes.

HEALTH CONDITIONS THAT AFFECT THE KIDNEYS

ALPORT'S SYNDROME	END-STAGE RENAL DISEASE (ESRD)
GLOMERULONEPHRITIS	GLOMERULOSCLEROSIS
GOODPASTURE'S SYNDROME	HEMOLYTIC UREMIC SYNDROME
HEPATORENAL FAILURE	HORSESHOE KIDNEY
HYDRONEPHROSIS	kidney cyst
MINIMAL CHANGE DISEASE	NEPHRITIS
NEPHROLITHIASIS	NEPHROPATHY of DIABETES
nephropathy of HYPERTENSION	NEPHROTIC SYNDROME
POLYCYSTIC KIDNEY DISEASE	pyelonephritis
RENAL CANCER	RENAL FAILURE
renal osteodystrophy	RENAL TUBULAR ACIDOSIS
rhabdomyolysis	WILMS'S TUMOR

For further discussion of the kidneys within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also BLADDER; ERYTHROCYTE; HEMATOPOIESIS; HORSESHOE KIDNEY; RETICULOCYTE; URETHRA.

kidney stone See NEPHROLITHIASIS.

kidney transplantation A surgical OPERATION to place a healthy, functioning kidney into a person whose own kidneys have permanently failed. The first successful kidney transplantation took place between identical twin brothers in 1954. However, until the discovery of the immunosuppressive DRUG cyclosporine in 1983, the risk of organ rejection was very high, and kidney transplantation was a treatment of last resort. With current IMMUNOSUPPRESSIVE THERAPY the recipient of a transplanted kidney can expect to live 5 to 20 years or longer with relatively normal kidney function.

Since the mid-1980s kidney transplantation has become the standard of treatment for END-STAGE RENAL DISEASE (ESRD), also called permanent kidney failure (RENAL FAILURE). Transplant surgeons in the United States perform about 15,000 kidney transplant operations each year. However, a severe

shortage of donor kidneys limits the availability of kidney transplantation. Another 30,000 to 45,000 people are eligible for kidney transplantations and await donor organs. A donor kidney may be a cadaver organ donation (donated after a person's death) or come from a person who has two healthy kidneys and offers to donate one to the recipient.

In the United States, the federal health-care program Medicare pays for 80 percent of most expenses related to kidney transplantation for those who meet the qualification criteria. The U.S. Centers for Medicare and Medicaid Services Web site (www.cms.hhs.gov) provides comprehensive information about eligibility and covered services. Private health insurance and other public programs also provide coverage for kidney transplantation costs, though coverage varies among carriers and programs.

Donor Kidneys

The primary source of donor kidneys is cadaver donation—people who authorize the donation of their organs when they die. In the United States the United Network for Organ Sharing (UNOS) administers the nationwide cadaver donor organ collection and distribution program, the Organ Procurement and Transplantation Network (OPTN). People eligible for kidney transplantation register with OPTN through regional organ transplantation centers. OPTN follows strict guidelines intended to ensure equitable access to donor organs. People may wait several months to several years for a matched cadaver donor kidney, as the OPTN system distributes organs to matched recipients who are the sickest.

The wait time for a living donor kidney transplant is typically significantly shorter, often only several months, because as soon as the transplant team confirms the intended donor is a match the surgeries (donation and transplantation) can take place. Living organ donation does not fall within OPTN. Only the intended recipient may receive the kidney from the living donor. The living donor is often a family member though may be a stranger who is a strong match with the recipient.

Donor-Recipient Match

The donor kidney must match the recipient as closely as possible in three ways. First, the donor and the recipient must have the same BLOOD TYPE. Second, the donor and the recipient must match HUMAN LEUKOCYTE ANTIGENS (HLAS), which are proteins on the surfaces of leukocytes (white BLOOD cells), as closely as possible. Every person has six HLAs. The more HLAs that match between donor and recipient, the higher the likelihood that the recipient's body will accept the donor kidney (though all organ transplant recipients take lifelong immunosuppressive therapy). Transplant surgeons like to see a match of three or more HLAs. Third, the donor's blood must not initiate an ANTIBODY response with the recipient's blood (called a negative crossmatch), which the transplant team tests by mixing samples of blood from each in a test tube.

Surgical Procedure

The transplant surgery generally takes three to five hours. With the person under general ANESTHESIA, the transplant surgeon makes an incision in the lower abdomen, placing the donor kidney in the abdominal cavity below the native kidneys. The surgeon attaches the donor kidney's arteries and veins to the recipient's iliac ARTERY and iliac VEIN, respectively, and the donor kidney's URETER to the BLADDER. Depending on the reason for the ESRD, the surgeon may either leave or remove the recipient's nonfunctioning kidneys. After returning to full consciousness in the recovery room, the recipient typically remains in the hospital for three to five days. The transplanted kidney may begin functioning immediately or take several weeks. The recipient undergoes RENAL DIALYSIS until kidney function becomes adequate.

Risks and Complications

The risks of transplantation surgery include bleeding during or after the operation and postoperative INFECTION. Because the transplanted kidney is lower in the abdomen than the native kidneys it lacks the protection of the rib cage and is more vulnerable to traumatic injury. Rarely the recipient's body may immediately reject the donor organ, in which case the transplant team must operate again to remove it. Most people recover fully from the surgery without complications, though there is always the risk of organ rejection. Many kidney transplant recipients experience episodes of organ rejection that the transplant

doctor can treat with various medications. The IMMUNOSUPPRESSIVE THERAPY that is necessary for organ transplant recipients to take lowers the body's overall immune response, lowering resistance to infection. IMMUNOSUPPRESSIVE MEDICATIONS have numerous other side effects as well. People who take long-term immunosuppressive therapy do have an increased risk for LYMPHOMA, a type of cancer that affects the lymph nodes.

Outlook and Lifestyle Modifications

Most people who receive transplanted kidneys feel better immediately after surgery and enjoy relatively normal lifestyles after recovering from surgery; however, they must continue taking immunosuppressive medications and receive regular medical checkups to monitor the health of their transplanted kidneys. Doctors generally recommend that people who have transplanted kidneys avoid activities with increased risk for blunt trauma to the abdomen, such as contact sports. The doctor may further recommend specific dietary and lifestyle modifications to maintain optimal kidney function.

See also ORGAN TRANSPLANTATION; SURGERY BENEFIT AND RISK ASSESSMENT.

Medicare coverage for permanent renal failure Federal government funding in the United States that pays for medical treatment for people of any age who have END-STAGE RENAL DISEASE (ESRD), also called permanent RENAL FAILURE. Though for other health conditions an individual must be age 65 or older to qualify for Medicare coverage, the US Congress in 1973 passed legislation broadening Medicare coverage to include care for ESRD at any age. There are specific eligibility requirements and co-payments. Health-care providers that offer care for ESRD have information about the application and approval processes. The US Centers for Medicare and Medicaid Services Web site (www.cms.hhs.gov) also provides comprehensive information about eligibility and covered services.

See also KIDNEY TRANSPLANTATION; QUALITY OF LIFE; RENAL DIALYSIS.

micturition See URINATION.

minimal change disease A disorder of kidney function in which the structure of the KIDNEYS, notably the nephrons, appears normal with regular (light) microscope examination though slightly abnormal with electron microscope examination. Minimal change disease is primarily a condition of childhood (usually in children under age six) and seldom occurs in adults. Researchers believe the condition is one of immune dysfunction in which T-cell lymphocytes cause molecular damage to the delicate walls of the glomeruli. The damage allows ALBUMIN (protein) to leak from the BLOOD into the URINE (ALBUMINURIA).

Symptoms and Diagnostic Path

The symptoms of minimal change disease are often vague and include

- edema, often of the face
- fatigue
- MUSCLE-wasting
- impaired growth
- unexplained weight gain

The diagnostic path begins with urinalysis, which typically shows albuminuria (albumin excretion). Other laboratory tests are often normal. There is a high correlation between minimal change disease and NEPHROTIC SYNDROME, a constellation of symptoms that indicate kidney dysfunction. The urologist may recommend a trial of treatment before conducting further, more invasive diagnostic procedures.

Treatment Options and Outlook

Treatment for minimal change disease is IMMUNOSUPPRESSIVE THERAPY with CORTICOSTEROID MEDICATIONS such as prednisone. Most children improve remarkably within two weeks, and nearly all within six to eight weeks. The nephrologist may make dietary recommendations to maintain appropriate protein, sodium, and fluid intake. Minimal change disease fully resolves, without residual damage to the kidneys, with treatment in most children. About 10 percent of children experience periodic RECURRENCE of symptoms through ADOLESCENCE and sometimes into adulthood. Children taking corticosteroid medications have a somewhat increased risk for INFECTION during the course of therapy.

Risk Factors and Preventive Measures

Because researchers do not know what causes minimal change disease, there are no measures to prevent its occurrence. Prompt treatment mini-

mizes the risk for permanent damage to the kidneys.

See also GLOMERULONEPHRITIS; GLOMERULOSCLEROSIS; NEPHRON.

nephrectomy A surgical OPERATION to remove a kidney. The most common reasons for nephrectomy are to treat RENAL CANCER, to remove a kidney for live donor KIDNEY TRANSPLANTATION, and to remove a kidney that is severely injured due to trauma or malformed due to CONGENITAL ANOMALY. There are three kinds of nephrectomy:

- partial nephrectomy, in which the surgeon removes only a portion of the kidney
- simple nephrectomy, in which the surgeon removes the entire kidney though leaves the surrounding tissue intact
- radical nephrectomy, in which the surgeon removes the kidney, surrounding tissues, and adjacent lymph nodes

Nephrectomy may be an open surgery, in which the surgeon operates through a large incision in the flank (side of the back), or laparoscopic, in which the surgeon operates through multiple small incisions using a laparoscope.

Surgical Procedure

Nephrectomy takes place in a hospital operating room with the person under general ANESTHESIA. For open nephrectomy, the surgeon makes a large incision into the flank over the kidney. The incision gives access to the kidney without the need to penetrate the peritoneum, as the KIDNEYS lie behind this protective membrane. The surgeon sutures off the renal ARTERY and VEIN and the URETER, then carefully cuts the kidney away from the adipose tissue that surrounds it and holds it in place. When the operation is radical nephrectomy for renal cancer, the surgeon also removes the adipose tissue, nearby connective tissue, and adjacent lymph nodes. After removing the kidney the surgeon sutures closed the incision, which will heal into a SCAR. Open nephrectomy takes two to four hours.

For laparoscopic nephrectomy, also called minimally invasive nephrectomy, the surgeon makes four or five small incisions, called ports, in locations around the flank on the side where the kidney will be removed. The surgeon inserts the laparoscope through one of the ports, and uses another to inflate the interior of the abdomen with a gas. The surgeon inserts instruments through the remaining ports. The laparoscope has a light and camera on the tip that conveys the image of the interior abdomen to a closed-circuit television monitor. The surgeon operates by watching the monitor. When the kidney is free from its BLOOD supply and connecting tissues, the surgeon inserts a special bag through one of the ports and puts the kidney into it. The surgeon carefully delivers the bag through the port, enlarging the port if necessary. When the kidney is out, the surgeon removes the instruments and laparoscope from their ports and sutures them closed. The ports heal into small scars. Laparoscopic nephrectomy takes three to five hours.

After either type of surgery, the person remains in the recovery room until fully awakened from the anesthesia and then goes to a hospital room. The hospital stay for open nephrectomy is generally five to seven days and for laparoscopic nephrectomy is generally three to five days. A person who undergoes open nephrectomy typically returns to regular activities in 8 to 12 weeks. A person who undergoes laparoscopic nephrectomy typically returns to regular activities in five to six weeks.

Risks and Complications

The primary risks of nephrectomy are bleeding and INFECTION, along with the potential for complications arising from anesthesia. These are uncommon events. The doctor will prescribe ANALGESIC MEDICATIONS to relieve postoperative PAIN. Further risks depend on the reasons for the nephrectomy. Some people experience fluctuations in BLOOD PRESSURE during the first few days after the nephrectomy, as the kidneys are key to regulating blood pressure in the body. This nearly always stabilizes without the need for treatment.

Outlook and Lifestyle Modifications

Most people fully recover and return to their regular activities after nephrectomy. The remaining kidney, if healthy, can more than adequately sustain the body's needs. People who have renal cancer often undergo follow-up CHEMOTHERAPY or RADIA-

TION THERAPY after surgery. The doctor may recommend dietary changes and other lifestyle modifications, depending on the person's general health status. A single kidney provides more than adequate function for people who are otherwise in reasonably good health. Lifestyle factors such as nutritious EATING HABITS, daily physical exercise, and maintaining healthy weight reduce strain on the kidney as well as the risk for HYPERTENSION (high blood pressure) and DIABETES, the two health conditions that are most likely to cause kidney disease.

See also MINIMALLY INVASIVE SURGERY; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

nephritis INFLAMMATION of the kidney. The most common causes of nephritis are bacterial INFECTION, which generally cause acute (sudden onset) nephritis, and AUTOIMMUNE DISORDERS, which tend to cause chronic or recurrent inflammation. Nephritis can be acute (come on suddenly), chronic (long-term), or recurrent (repeated episodes of acute nephritis). Chronic nephritis can lead to NEPHROPATHY.

Bacterial nephritis When infection involves the glomeruli, it is infectious GLOMERULONEPHRITIS. Infectious glomerulonephritis develops as a complication of untreated or undertreated STREP THROAT or other streptococcal infection elsewhere in the body. Occasionally another bacterial strain such as staphylococcus is responsible. Infection that travels up the ureters from the BLADDER as a complication of untreated or undertreated URINARY TRACT INFECTION (UTI) is pyelonephritis. In pyelonephritis the infection involves the pelvis of the kidney where URINE drains from the kidney into the ureters. VESICOURETERAL REFLUX, in which urine backflows from the bladder through the ureters to the kidneys, is a common cause of pyelonephritis.

Interstitial nephritis In interstitial nephritis the inflammation affects the spaces between the tubules in the nephrons. Such inflammation is nearly always a consequence of acute toxic nephropathy. Medications such as penicillin and penicillin-derived antibiotics, the diuretic medication furosemide and thiazide diuretics, and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) are commonly responsible for acute interstitial nephritis. The nephritis generally resolves without lingering complications within a few weeks of stopping the medication.

Lupus nephritis The autoimmune disorder SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) affects the KIDNEYS in about 40 percent of people who have SLE. In some people, lupus nephritis may be the only manifestation of SLE. Lupus nephritis can progress rapidly to RENAL FAILURE and END-STAGE RENAL DISEASE (ESRD). Because women who have SLE outnumber men who have SLE nearly nine to one, lupus nephritis far more commonly affects women.

Hereditary nephritis Hereditary nephritis is a genetic disorder that results from GENE mutations. The symptoms of hereditary nephritis are apparent at or shortly after birth, and the inflammation tends to be progressive. The most frequent presentation of hereditary nephritis is ALPORT'S SYNDROME, a disorder of protein encoding.

Symptoms and Diagnostic Path

The symptoms of nephritis may include

- HEMATURIA (bloody urine)
- OLIGURIA (diminished urine volume)
- edema (fluid retention that causes swelling in the tissues), notably of the face, hands and arms, and legs and feet
- loss of APPETITE, NAUSEA, and VOMITING
- FEVER (bacterial nephritis)

The diagnostic path begins with urinalysis and BLOOD tests that assess kidney function. Urinalysis may show the presence of BACTERIA, indicating the cause of the nephritis is infection. Other diagnostic procedures the nephrologist may choose to conduct include further blood and urine tests, ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and kidney biopsy. The biopsy shows the presence of inflammation and any damage that has occurred to the tubules or glomeruli.

Treatment Options and Outlook

Treatment depends on the underlying cause. Bacterial nephritis requires antibiotic therapy, often long term (up to six months). Severe infection requires hospitalization for intravenous ANTIBIOTIC MEDICATIONS. Most people recover fully and without residual damage from bacterial nephritis.

Because the kidneys play key roles in regulating BLOOD PRESSURE kidney disease that interferes with such functions can result in HYPERTENSION (high blood pressure), which requires treatment. The doctor may recommend dietary changes to limit sodium, protein, and water intake. Treatment for lupus nephritis often includes IMMUNOSUPPRESSIVE THERAPY.

Risk Factors and Preventive Measures

The primary risk factors for nephritis are the conditions that can cause it. Nephrotoxins are generally avoidable once the doctor identifies them as responsible for the nephritis. Bacterial infections nearly always migrate to the kidneys from elsewhere in the body. Early and appropriate treatment for the primary infection, particularly strep throat, helps prevent the infection from spreading to the kidneys.

See also GLOMERULONEPHRITIS; GLOMERULOSCLEROSIS; INHERITANCE PATTERNS; NEPHROPATHY; NEPHROTIC SYNDROME.

nephrolithiasis The formation of calcifications (also called calculi) in the KIDNEYS, usually called kidney stones. Kidney stones are common, with about 1 in 10 adults in the United States likely to have at least one over the course of adulthood. Some people pass kidney stones with little discomfort and may not even be aware of them, though for many people nephrolithiasis is extremely painful and debilitating. Kidney stones may lodge in the ureters or within the kidney, usually in the renal pelvis or a structure within the renal medulla called the calyx where the collection tubules empty their URINE.

Kidney stones that block the flow of URINE constitute a medical emergency that may require immediate treatment.

About 75 percent of kidney stones are made of calcium in combination with oxalate, phosphate, or carbonate. Calcium oxalate stones are the most common. About 10 percent of stones are made of uric acid and occur most frequently in men who have GOUT (a form of arthritis) or in people who are undergoing CHEMOTHERAPY. Other stones may form of cystine, an amino acid compound, or of struvite, a compound of magnesium, ammonia, and phosphate that tends to form in women who have frequent bacterial urinary tract infections (UTIs).

Symptoms and Diagnostic Path

Common symptoms of kidney stones include

- rapid onset of excruciating PAIN in the side (flank) or back
- persistent or colicky (wavelike) ABDOMINAL PAIN
- NAUSEA and VOMITING
- URINARY FREQUENCY and URINARY URGENCY
- FEVER and chills
- NOCTURIA (urination at night)
- groin pain in men or women or testicular pain in men

The diagnostic path may include abdominal X-RAY, ULTRASOUND, OR COMPUTED TOMOGRAPHY (CT) SCAN to detect the location of the stone. The doctor may also choose to conduct an INTRAVENOUS PYELOGRAM (IVP) to assess the extent to which a stone is blocking the flow of BLOOD or urine. Blood and urine tests may show elevated levels of calcium, uric acid, or oxalate.

Treatment Options and Outlook

Treatment for nephrolithiasis with severe pain begins with analgesic medication, often narcotic, to relieve the pain. Further treatment to move the stone out of the urinary tract may include EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL), a noninvasive method that effectively disperses stones up to 2 centimeters in diameter, or surgery such as percutaneous lithotomy in which the nephrologist uses laparoscopic surgery to snare and remove the stone. Most urologists prefer to take a course of watchful waiting with calculi that are not causing symptoms or that appear small enough to be able to pass through the urinary tract on their own, often recommending increased water consumption to increase the volume of the urine.

Kidney stones tend to recur, so often it is useful to determine the stone's composition, as this helps the nephrologist or urologist assess appropriate measures to reduce the risk for future stone formation. The doctor will likely recommend strain-

ing the urine to capture the stones or stone fragments when they pass, for laboratory analysis. Despite the pain they cause, kidney stones do not usually cause permanent damage to the kidneys.

People who have had kidney stones should make dietary modifications, such as calcium restriction, only if the doctor specifically recommends them. Though doctors once believed dietary calcium was a key culprit in the development of kidney stones, recent research shows that when blood levels of calcium are too high (HYPERCALCEMIA) the cause is more likely to be overabsorption from the gastrointestinal tract than excessive consumption. Cutting back on dietary calcium in such a situation can have the opposite and undesired consequence of increasing gastrointestinal absorption of calcium. Dietary calcium is essential for BONE STRENGTH and health, tissue HEALING, and proper NERVE and MUSCLE function.

Risk Factors and Preventive Measures

Men are more likely than women to develop kidney stones. As well, kidney stones appear to run in families, suggesting a genetic or hereditary component. People who have RENAL TUBULAR ACIDOSIS or INFLAMMATORY BOWEL DISEASE (IBD) have increased risk for developing nephrolithiasis. Lifestyle measures to reduce the risk for kidney stones include drinking six to eight 8-ounce glasses of water and getting physical exercise daily. These measures increase the volume of urine, helping dissolve minerals that might crystallize, and keeps the urine moving through the urinary system. The doctor may prescribe medication to reduce the risk of kidney stones in people who have history of RECURRENCE.

See also CYSTINURIA; HYPEROXALURIA; MINIMALLY INVASIVE SURGERY; URINARY TRACT INFECTION (UTI); UROLITHIASIS.

nephron The microscopic functional unit of the kidney. Each kidney contains more than a million nephrons, each of which extends from the renal cortex into the renal medulla in fairly linear fashion. Two elements make up the nephron: the renal tubules and the renal corpuscle. The renal corpuscle contains the GLOMERULUS, the coiled network of capillaries that bring BLOOD into the nephron, and Bowman's capsule, the podlike structure that encases the glomerulus. The pressure of the blood as it enters the glomerulus forces molecules of water, electrolytes, and other substances through the thin glomerular wall into Bowman's capsule. This mixture, called filtrate, collects in the capsule and drains into the renal tubule. Each segment of the tubule reabsorbs different substances from the filtrate as it passes through them. A second network of capillaries separate from the glomerulus, the peritubular capillaries, entwines the renal tubule to allow the reabsorbed materials to reenter the blood circulation.

The first portion of the tubule to exit Bowman's capsule, the proximal tubule (also called the proximal convoluted tubule), runs along the renal corpuscle, heading inward toward the renal medulla though it remains within the renal cortex. The proximal tubule reabsorbs about two thirds of the sodium and two thirds of the water the filtrate contains, and reabsorbs calcium when vitamin D is present. The next segment, the loop of Henle, drops deep into the renal medulla, makes a sharp loop, and rises back up into the renal cortex in somewhat of a hairpin appearance. Different portions of the loop of Henle reabsorb sodium, potassium, chloride, magnesium, calcium, and water. The loop of Henle plays a significant role in the concentration and dilution of the URINE, and is the target of some types of diuretic medications. The distal tubule (also called the distal convoluted tubule) continues up through the renal cortex and wraps around the renal corpuscle, ultimately joining with the collecting tubule (also called the collecting duct). The distal tubule reabsorbs sodium and bicarbonate and secretes potassium. The final segment of the renal tubule is the collecting tubule, which funnels the remaining filtrate toward the renal pelvis for excretion via the URETER as urine. Only water reabsorption takes place from the collecting tubule.

For further discussion of the nephron within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also BLADDER; FANCONI'S SYNDROME; KIDNEYS; URETHRA.

nephropathy Progressive, irreversible damage to the KIDNEYS that occurs as a result of systemic

health conditions or disease processes. Nephropathy is the main cause of END-STAGE RENAL DISEASE (ESRD) and the leading reason for KIDNEY TRANSPLANTATION. Doctors diagnose more than 100,000 Americans with nephropathy every year. DIABETES and HYPERTENSION (high BLOOD PRESSURE) are the leading cause of nephropathy in the United States. These conditions damage the delicate glomeruli, the capillary networks that feed BLOOD through the nephrons, the filtering structures of the kidneys. Each kidney contains more than a million nephrons and can tolerate the loss of about two thirds of them before symptoms of kidney failure become apparent. By such time, however, damage to the kidneys is usually profound.

Nephropathy of diabetes Diabetes accounts for 45 percent of kidney failure among Americans. The elevated GLUCOSE (sugar) levels in the blood that occur with diabetes are particularly damaging to the blood vessels and the nerves that serve them. For reasons researchers do not understand, African Americans, Hispanic Americans, and Native Americans who have diabetes are significantly more likely to develop nephropathy of diabetes (sometimes called diabetic nephropathy). About 40 percent of people who have diabetes develop some degree of nephropathy, half of whom eventually progress to ESRD. Nephropathy is more likely in type 1 diabetes.

Nephropathy of hypertension Hypertension accounts for 25 percent of nephropathy among Americans. Chronically elevated blood pressure places considerable stress against the walls of the glomeruli, causing microscopic ruptures and scarring (fibrosis). As with nephropathy of diabetes, nephropathy of hypertension (sometimes called hypertensive nephropathy) is significantly more likely to develop in African Americans, Hispanic Americans, and Native Americans. The progression to ESRD can be rapid in poorly controlled or untreated hypertension.

IgA nephropathy In IMMUNOGLOBULIN A (IgA) nephropathy, a dysfunction of the IMMUNE SYSTEM results in deposits of gA, a protein, accumulating within the tubules of the nephrons. The kidneys have no process for removing these deposits, which eventually clog the tubules and prevent them from transporting filtrate. IgA nephropathy typically is ongoing for 20 years or longer before causing enough damage to result in symptoms. Many people who have IgA nephropathy also have a systemic autoimmune disorder such as SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), RHEUMATOID ARTHRITIS, or ANKYLOSING SPONDYLITIS. Treating the underlying autoimmune disorder often slows the progression of the nephropathy.

Toxic nephropathy Many drugs and chemicals are nephrotoxins, substances that damage the kidneys. Toxic nephropathy typically develops as a result of chronic exposure though can occur with limited though substantial exposure (such as DRUG overdose). Common nephrotoxins include heavy metals (such as lead and cadmium), organic solvents (such as benzene), and certain ANTIBIOTIC MEDICATIONS (notably gentamicin and streptomycin, which are sometimes the only antibiotics effective against life-threatening infections such as bacterial MENINGITIS).

Worrisome culprits are the NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). DEHYDRATION in combination with NSAID use, which occurs among people who compete in ENDURANCE activities, is a particular risk. Long-term, daily use of other pain-relief medications, notably codeine and combination products that contain CAFFEINE with acetaminophen or aspirin, also can cause this form of toxic nephropathy, commonly called analgesic nephropathy. People who have conditions of chronic PAIN are most susceptible to analgesic nephropathy. People who have diabetes or congestive HEART FAILURE, have other kidney disease, engage in heavy ALCOHOL consumption, or are age 70 or older also have increased risk for analgesic nephropathy, in part because many people do not understand the danger regular analgesic use poses for the kidneys. These circumstances reduce kidney function, increasing the likelihood that further damage to the kidneys will result in kidney failure.

Symptoms and Diagnostic Path

Nephropathy generally does not show symptoms until damage to the kidneys is fairly advanced. One of the earliest indications of nephropathy is ALBUMINURIA, a consequence of protein leaking from the glomeruli into the filtrate. Doctors often detect albuminuria through urinalysis done as part of a routine medical examination. When symptoms do appear, they often include

- frothy URINE during URINATION (indicates albuminuria)
- edema (fluid accumulation in the tissues), most noticeable upon awakening and often affecting the face and the feet
- fatigue
- loss of APPETITE in combination with increased weight (weight gain results from edema)
- HEADACHE

Some forms of nephropathy also cause painless HEMATURIA (bloody urine). The diagnostic path includes further urine tests as well as BLOOD tests to assess kidney function. The nephrologist may perform a kidney biopsy to examine the nephrons under the microscope, which reveals the microscopic damage of nephropathy. The nephrologist may also conduct diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN and INTRAVENOUS PYELOGRAM (IVP) to examine kidney structure and function.

Treatment Options and Outlook

Treatment targets the underlying condition with the aim of slowing progression of the nephropathy and preserving remaining kidney function. It is critically important for people who have diabetes or hypertension (or both) to maintain effective control of these conditions through medication therapy and lifestyle measures. Some people are able to successfully manage the underlying condition and the nephropathy to avoid ESRD, though often nephropathy progresses to require RENAL DIALYSIS. Whether kidney transplantation is a viable treatment option for ESRD resulting from nephropathy depends on multiple factors, including co-existing health conditions, age, and overall health status.

Risk Factors and Preventive Measures

Diabetes and hypertension combined cause more two thirds of nephropathy in the United States. The risk for nephropathy is particularly high for people who have both these conditions. Preventing these conditions and appropriately and diligently treating them when they develop mitigates the risk for nephropathy. People who take long-term NSAIDs to treat chronic conditions such as OSTEOARTHRITIS should have regular blood and urine tests to screen for early indications of nephropathy, and work with their doctors to find the lowest effective DOSE and least nephrotoxic medication to manage the condition and its symptoms.

See also HEAVY-METAL POISONING; HEPATORENAL FAILURE; NEPHRITIS; NEPHRON; NEPHROTIC SYNDROME; RETINOPATHY.

nephrotic syndrome A constellation of symptoms that result as a consequence of conditions that damage the glomeruli within the renal nephrons. The damage allows excessive protein to move through the walls of the glomeruli into the filtrate. The tubules are unable to reabsorb the large protein molecules, so the body ends up excreting the protein in the URINE (ALBUMINURIA). The excessive excretion of protein results in HYPOALBUMINEMIA, or low levels of ALBUMIN in the BLOOD circulation. The hypoalbuminemia allows fluid to leave the blood circulation and enter the interstitial tissues, where it accumulates to cause edema (swelling). Because the blood volume is now low, the KIDNEYS compensate by reabsorbing higher levels of water and sodium.

Most people who have nephrotic syndrome have diagnosed kidney disease so the underlying cause is clear. When indications of nephrotic syndrome occur in someone who does not have kidney disease, the diagnostic path begins with blood and urine tests to assess kidney function. Further diagnostic procedures then strive to identify the underlying renal condition. Treatment targets the underlying renal condition as well as symptoms such as HYPERTENSION (high BLOOD PRESSURE) and RENAL FAILURE. Treatment may include RENAL DIALYSIS when renal function is significantly impaired. The outlook depends on the underlying renal condition and its response to treatment. Symptoms of nephrotic syndrome generally resolve when the underlying condition improves.

See also GLOMERULONEPHRITIS; GLOMERULOSCLEROSIS; MINIMAL CHANGE DISEASE; NEPHRITIS; NEPHRON; UREMIA.

nephrotoxins Substances such as medications or environmental chemicals that damage the glomeruli and the tubules within the nephrons of

the KIDNEYS. Among those most commonly associated with altered kidney function and RENAL FAILURE are

- heavy metals such as lead, mercury, cadmium, and arsenic; exposure to these metals is most often occupational
- NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen, naproxen, and ketoprofen
- possibly acetaminophen
- Contrast dyes used in radiologic procedures
- certain ANTIBIOTIC MEDICATIONS, notably streptomycin and gentamicin
- organic solvents such as benzene

People who already have compromised kidney function or conditions such as DIABETES or HYPERTENSION (high BLOOD PRESSURE) are at greater risk for kidney damage resulting from nephrotoxins. Chronic DEHYDRATION, such as may occur with diuretic therapy or insufficient water consumption, increases the risk for kidney damage resulting from medications, especially NSAIDs.

See also HEPATOTOXINS; NEPHRON; NEPHROPATHY.

neurogenic bladder A condition in which the nerves that control the BLADDER do not work properly, allowing the bladder to be underactive (hypotonic) or overactive (spastic). Damage may occur to the SPINAL CORD AND SPINAL NERVES, BRAIN, or PERIPHERAL NERVES that serve the bladder. Conditions that can cause such damage include traumatic injury, STROKE, degenerative neurologic disorders such as MULTIPLE SCLEROSIS and PARKINSON'S DISEASE, NEUROPATHY of DIABETES and neuropathy of HIV/AIDS, and injury to the nerves of the bladder as a consequence of pelvic surgery (such as PROSTATECTOMY in men or HYSTERECTOMY in women). URINARY INCONTINENCE is the most common consequence of neurogenic bladder.

The diagnostic path includes urinalysis, BLOOD tests, and diagnostic imaging procedures such as CYSTOSCOPY, ULTRASOUND, or COMPUTED TOMOGRAPHY (CT) SCAN. The urologist may also perform a voiding CYSTOURETHROGRAM to evaluate the flow of URINE through the urinary system. Electromyogram (EMG) measures the response of the nerves and muscles of the bladder and urethra to mild electrical stimuli. Other tests can measure the capacity and rate of emptying of the bladder.

Treatment targets the underlying cause of the neurogenic bladder when possible. Other treatment measures aim to improve urinary incontinence. The success of the treatment often depends on the underlying cause. Various medications may increase or decrease the bladder's responses. Surgery is sometimes an option. Though it may take time and much trial and error, most people find acceptable measures for accommodating neurogenic bladder.

See also SPINAL CORD INJURY; TRAUMATIC BRAIN INJURY (TBI); URINARY TRACT INFECTION (UTI).

nocturia The need to get up from nighttime sleep to urinate. Nocturia is a significant cause of SLEEP DISORDERS though has numerous potential causes. Nocturia becomes more common with increasing age in both women and men, sometimes simply as a consequence of normal age-related changes that occur in the urinary tract. Key among these changes is the reduced ability of the BLADDER to distend because lost elasticity in the tissues, effectively shrinking the bladder's capacity.

Many people are unaware how much fluid they drink in the evening. The urinary system is still processing all this fluid when the person lies down to go to bed. Often, simply changing habits to minimize fluid consumption after dinner is enough to slow URINE production through the night. When nocturia persists despite such measures, the urologist may prescribe medications such as tolterodine or oxybutynin that slow the bladder's response.

CONDITIONS FOR WHICH NOCTURIA IS A COMMON SYMPTOM

BENIGN PROSTATIC HYPERPLASIA (BPH)	CYSTITIS
CYSTOCELE	HYDRONEPHROSIS
NEPHROLITHIASIS	NEUROGENIC BLADDER
PROSTATITIS	URINARY TRACT INFECTION (UTI)
UROLITHIASIS	VAGINITIS

See also AGING, URINARY SYSTEM CHANGES THAT OCCUR WITH; ENURESIS; URINARY INCONTINENCE.

oliguria Significantly reduced URINE production that occurs as a consequence of RENAL FAILURE, DEHYDRATION, hemorrhage (massive BLOOD loss), or SHOCK. Normal adult urinary output is 1500 milliliters to 3000 milliliters per day. In oliguria urinary output is 500 ml per day or less. Oliguria indicates that the KIDNEYS are not receiving enough blood or are not functioning to filter the blood. Unless urine output increases, toxins will accumulate in the blood and the circumstance may become life-threatening.

See also ANURIA; UREMIA.

P

percutaneous lithotripsy See EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL).

polycystic kidney disease An inherited disorder in which hundreds to thousands of cysts form in the KIDNEYS as well as in other organs and structures such as the LIVER, HEART, and BRAIN. The cysts greatly enlarge and deform the kidneys. The cysts arise from the nephrons, which they destroy as they grow. Polycystic kidney disease affects about 500,000 people in the United States and is the fourth-leading cause of END-STAGE RENAL DISEASE (ESRD). About 10 percent of people on long-term RENAL DIALYSIS have polycystic kidney disease.

The most common type of polycystic kidney disease is autosomal dominant, which affects more than 90 percent of people who have the condition. It occurs as the result of mutations in the PKD1 GENE located on CHROMOSOME 16 and the PKD2 gene on chromosome 4. GENETIC TESTING can detect the presence of these mutations, which confirms the diagnosis. The progression of kidney damage in autosomal dominant polycystic kidney disease typically takes place over decades, with symptoms beginning to manifest around age 30 to 40. A much less common type of polycystic kidney disease is autosomal recessive, which has a different clinical presentation and course of disease. Its symptoms are often present at birth or appear in early childhood.

Symptoms and Diagnostic Path

Autosomal dominant polycystic kidney disease typically shows no symptoms until the person is age 30 to 40. At that time the cysts become numerous enough and large enough to cause PAIN and disrupt kidney function. Urinary system symptoms that emerge include

- HEMATURIA (bloody URINE)
- frequent, recurrent URINARY TRACT INFECTION (UTI)
- kidney stones (NEPHROLITHIASIS)
- upper ABDOMINAL PAIN

Additional symptoms include HYPERTENSION (high BLOOD PRESSURE) resulting from damage to the kidneys and cysts in the liver and other organs. Diverticulosis, a gastrointestinal condition in which small pockets distend from the bowel, is also common. Some people may have deformed heart valves and deformities in blood vessels that cause aneurysms to develop.

Treatment Options and Outlook

Treatment focuses on relieving symptoms. ANTIBIOTIC MEDICATIONS are necessary to treat a UTI. Surgery may be necessary to repair any ANEURYSM and sometimes to reduce the size of the kidneys. Most people progress to ESRD within 10 years of the appearance of symptoms, at which time renal dialysis becomes necessary to sustain life. KIDNEY TRANSPLANTATION is often a viable treatment option. The transplanted kidney does not develop cysts. However, cysts do continue to develop in other organs.

Risk Factors and Preventive Measures

Polycystic kidney disease is both genetic and inherited. People who have this condition in their families may benefit from genetic testing to determine whether they carry the mutated genes, and to discuss their family planning options with a genetic counselor.

See also INHERITANCE PATTERNS; RENAL CYST.

proteinuria See ALBUMINURIA.

pyelonephritis See NEPHRITIS.

renal cancer The growth of a malignant (cancerous) tumor in the kidney. Doctors diagnose about 30,000 people in the United States with renal CANCER, also called kidney cancer, each year. Men are twice as likely as women to get renal cancer, and cigarette smokers (male or female) are two to four times as likely as nonsmokers to get renal cancer. The most common form of renal cancer is renal cell CARCINOMA (RCC), which accounts for more than 90 percent of RCC among Americans. RCC arises from the epithelial cells that line the tubules within the nephrons. A type of kidney tumor that occurs almost exclusively in children under age eight is WILMS'S TUMOR, also called nephroblastoma. Though Wilms's tumor also arises from the tubules, its cells, course of growth, and treatment options are unique. Cancer from other sites may metastasize to the kidneys.

Symptoms and Diagnostic Path

The earliest indication of renal cancer is HEMATURIA (BLOOD in the URINE), which may be gross (enough blood is present to discolor the urine) or microscopic (the laboratory detects erythrocytes in the urine during examination of the urine sample under the microscope). Other symptoms may include

- lump or swelling in the central abdomen
- fatigue
- abdominal or back PAIN not related to injury
- unexplained or unintended weight loss

STAGING OF RENAL CANCER

Renal Cancer Stage	Extent of Cancer Treatment	Protocols/Options
stage 1	tumor remains confined to one site in one kidney and is 7 cm or smaller	partial or simple NEPHRECTOMY
stage 2	tumor extends beyond the tissue capsule surrounding the kidney or is larger than 7 cm	radical nephrectomy
stage 3	tumor extends to adjacent lymph nodes or the veins that carry BLOOD from the kidney	radical nephrectomy biological therapy
stage 4	tumor extends to both kidneys or to other organs in the abdomen or to distant organs such as the LUNGS or BRAIN	palliative surgery palliative therapies
recurrent	tumor returns after treatment, appearing either in the same kidney (when first cancer was stage 1), the other kidney, or another location in the body	varies according to previous treatment

- edema (swelling due to retained fluid in the tissues), notably in the hands and feet

The diagnostic path begins with urine tests, blood tests, and abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN. Biopsy of the detected tumor confirms the diagnosis and provides information about whether the cancer has yet metastasized. The pathologist assigns the cancer a stage based on the appearance and behavior of its cells. The cancer's stage determines the appropriate treatment options and expected outcome of treatment.

Treatment Options and Outlook

Treatment depends on multiple factors including the person's age, overall health status, and location and stage of the cancer. Doctors generally prefer surgery (NEPHRECTOMY) to remove the tumor (stage 0) or the kidney (all other stages). The nephrectomy may be segmental (removal of only the tumor and a small margin of healthy tissue), simple (removal only of the kidney), or radical (removal of the kidney, surrounding tissue, and adjacent LYMPH NODES). CHEMOTHERAPY and RADIATION THERAPY are not very effective in treating renal cancer. Biological therapies such as INTERFERONS and INTERLEUKINS, which stimulate the IMMUNE SYSTEM to step up its attack against the cancer cells, are showing great promise in renal cancer. The oncologist may use biological therapy after surgery for renal cancers that are stage 3 and 4. Some studies suggest a combination of biological therapy and chemotherapy may be more effective than biological therapy alone in some people. Treatment for recurrent renal cancer depends on how and where the cancer returns as well as on previous treatment.

Risk Factors and Preventive Measures

Cigarette smoking is the most identifiable, as well as preventable, risk for renal cancer. Other lifestyle factors that raise an individual's risk for renal cancer include lack of physical exercise (sedentary lifestyle) and OBESITY. Researchers believe obesity alters hormonal activity in the body in ways that facilitate the growth of renal cell carcinoma. Other known risks for renal cancer include POLYCYSTIC KIDNEY DISEASE, exposure to asbestos, exposure to heavy metals such as arsenic and cadmium, and industrial chemicals such as benzene and trichloroethylene. Renal cancer is also more common in people between the ages of 50 and 70, and in people who have a family history of renal cancer. The latter suggests genetic involvement, though researchers have yet to confirm evidence of this.

See also ASBESTOSIS; BLADDER CANCER; KIDNEYS; NEPHRON; NEUROTOXINS; PROSTATE CANCER.

renal cyst An encapsulated, fluid-filled growth that occurs in the kidney. Simple renal cysts are common and nearly always benign (noncancerous). Complex renal cysts, which may contain calculi (stones) and BLOOD, may be benign or cancerous. Most renal cysts, simple or complex, do not cause symptoms. Rather, the doctor detects them during diagnostic procedures, such as abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, to evaluate other health concerns. When symptoms do occur, they may include a sensation of pressure if the cyst is large enough to pressure other structures in the abdomen or interfere with kidney function. Occasionally, a renal cyst grows large enough or in a location to cause significant PAIN.

Ultrasound or CT scan generally provides enough information for the nephrologist to determine whether a renal cyst appears suspicious. A needle biopsy, which removes a small sample of tissue and fluid from the cyst, can show whether the cyst is cancerous. The nephrologist may recommend a course of watchful waiting for benign cysts that cause no symptoms. Surgery is necessary to remove symptomatic or cancerous cysts. Recovery from such surgery—which may be laparoscopic or open, depending on the size and location of the cyst—is generally complete and without complications. The presence of multiple cysts may indicate POLYCYSTIC KIDNEY DISEASE, a genetic disorder in which numerous cysts form in the KIDNEYS as well as in other organs. Recurrent cysts require further evaluation.

See also NEPHROLITHIASIS; RENAL CANCER.

renal dialysis Procedures to filter toxins from the BLOOD when the KIDNEYS are unable to perform this function. Renal dialysis can be short term or

long term. Though in theory renal dialysis could sustain life indefinitely, in practice most people experience a steady decline of overall health with long-term dialysis because artificial methods of cleansing toxins from the blood are not as effective, efficient, or thorough as the natural processes the kidneys perform. However, it is not uncommon for people to use renal dialysis for 10 to 20 years or longer. There are two general types of renal dialysis: hemodialysis and peritoneal dialysis.

Hemodialysis

Hemodialysis filters toxins directly from the blood. The person goes to a hemodialysis center for each dialysis treatment. A catheter inserted into a blood vessel, usually in the arm, routes the blood circulation externally through a machine that removes toxins. The cleansed blood then returns to the body through a second catheter. When hemodialysis is long term, the doctor places a permanent arteriovenous (AV) shunt that connects an ARTERY and a VEIN. The dialysis machine's cannulas then connect to the shunt.

The hemodialysis machine consists of a pump and a container, called the dialyzer with a semiporous membrane inside. The membrane looks somewhat like the filter inside a water purification canister. On one side of the membrane is a solution called the dialysate. The dialyzer pumps blood into the container on the other side of the membrane. The dialysate attracts certain substances—minerals, electrolytes, and waste byproducts—to cross the membrane from the blood. The dialysate absorbs these substances. Fresh dialysate circulates through the dialyzer at the same rate as the blood. The blood and the dialysate never come into direct contact with one another. Another type of filter traps any air bubbles that are in the blood before the blood returns to the body. The dialyzer holds only a few ounces of blood at a time. It takes three to five hours for the blood to circulate through the dialyzer enough times to remove an appropriate amount of waste and toxins. Most people need three hemodialysis sessions every week.

In the United States hemodialysis is the standard renal dialysis method. Many nephrologists feel it more thoroughly cleanses the blood. However, hemodialysis entails significant risks. Key among these risks are INFECTION with HEPATITIS and other bloodborne conditions, injury to the blood vessels used to shuttle blood between the person and the dialysis machine, and microscopic damage to the blood cells.

Peritoneal Dialysis

Peritoneal dialysis makes use of a natural membrane in the body, the peritoneum, which encloses the abdominal cavity. Peritoneal dialysis is a continuous process. Two catheters surgically inserted into the abdominal cavity serve as the portals through which dialysate enters and leaves the cavity. The doctor prescribes the dialysate, which comes premixed in single-DOSE bags.

The molecules of the dialysate are to large to pass through the peritoneum so the solution remains contained in the abdominal cavity. The blood's natural circulation carries blood through the blood vessels (capillary networks) within the peritoneum. As with hemodialysis, the dialysate attracts certain molecules to cross the membrane into the dialysate. A second catheter carries dialysate out of the abdominal cavity. There are two stages to peritoneal dialysis, the exchange (draining the dialysate into and out of the abdominal cavity) and the dwell (the time during which the dialysate remains in the abdominal cavity.

There are two types of peritoneal dialysis:

- Continuous ambulatory peritoneal dialysis (CAPD) instills dialysate into the abdominal cavity using gravity to pull the dialysate into the catheter. The dialysate remains in the abdominal cavity for about four hours, then the person drains it out through the second catheter. Most people who use this method need four treatments each day. Aside from the 30 minutes it takes to instill the dialysate and the 30 minutes it takes to drain the dialysate, the person is unencumbered and goes about his or her regular activities.
- Continuous cycler-assisted peritoneal dialysis (CCPD) uses a pump to rapidly infuse and extract the dialysate at night when the person is sleeping, with dwell times of about two hours. The person then infuses the abdominal cavity with dialysate upon awakening, and retains the solution all day for a single long dwell time.

The primary advantage of peritoneal dialysis is mobility. Most people are able to participate in regular activities, including work, while peritoneal dialysis is under way, provided the person can perform exchanges on the necessary time schedule and there is a hygienic, private location where the person can do the exchange. The success of peritoneal dialysis is more variable than that of hemodialysis because the permeability of the peritoneum varies among individuals. Some doctors believe peritoneal dialysis is less effective than hemodialysis at clearing toxins from the body.

Benefits and Risks of Renal Dialysis

Renal dialysis is the difference between life and death for people who have END-STAGE RENAL DISEASE (ESRD). For most people, the benefits clearly outweigh the potential risks and complications. The primary risks related to renal dialysis are infection, and, with hemodialysis, bleeding. Renal dialysis becomes less effective over time because it simply is not as effective as the body's natural mechanisms. A slow cascade of complications arises. Dialysis only cleanses the blood; it cannot restore kidney function or prevent further degeneration of the kidneys.

See also QUALITY OF LIFE.

renal failure The inability of the KIDNEYS to adequately filter toxins from the body. Generally the kidneys reach the point of renal failure when they have less than 15 percent functional capacity. Renal failure can be acute (occur suddenly) or chronic (develop slowly over time). Though the term *failure* implies the condition is permanent, but this is not necessarily the case. Most people who experience acute renal failure fully recover with appropriate treatment. When the deterioration of kidney function is progressive and irreversible, however, renal failure is not only permanent but also eventually becomes complete. This irreversible condition is END-STAGE RENAL DISEASE (ESRD). A person who has ESRD requires long-term RENAL DIALYSIS or KIDNEY TRANSPLANTATION to sustain life.

Acute renal failure Acute renal failure can occur in response to any circumstance that overwhelms the body, such as systemic INFECTION, severe BURNS, or a toxic assault such as a DRUG overdose or massive exposure to a nephrotoxin. DEHYDRATION and lack of BLOOD flow to the kidney (such as may occur with severe ATHEROSCLEROSIS or a blood clot) also can cause acute renal failure. Acute renal failure may require short-term renal dialysis to cleanse the blood while the kidneys recover as well as appropriate treatment for the cause of the renal failure.

COMMON CAUSES OF ACUTE RENAL FAILURE

acute NEPHRITIS	ALCOHOL poisoning
DEHYDRATION	DRUG OVERDOSE
extensive BURNS	gentamicin
HEART FAILURE	HEAT STROKE
HEMOLYTIC UREMIC SYNDROME	LIVER FAILURE
major surgery	multisystem failure
nephrotoxin exposure	reaction to contrast dye
renal ischemia	SEPTICEMIA
streptomycin	trauma

Chronic renal failure Chronic renal failure develops gradually over time, often years to decades. The most common causes of chronic renal failure are NEPHROPATHY of DIABETES and nephropathy of HYPERTENSION (high BLOOD PRESSURE). Other causes include long-term exposure to NEPHROTOXINS, long-term daily use of nephrotoxic drugs such as NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) and other ANALGESIC MEDICATIONS (PAIN relievers), notably codeine. Chronic renal failure may also consist of repeated bouts of acute renal failure that leave minor residual damage. Over time this damage becomes cumulative, causing scarring in the nephrons that impairs their ability to function. About 20 million Americans live with chronic renal failure.

COMMON CAUSES OF CHRONIC RENAL FAILURE

ALPORT'S SYNDROME	chronic HYDRONEPHROSIS
DIABETES	FANCONI'S SYNDROME
GLOMERULONEPHRITIS	GLOMERULOSCLEROSIS
GOODPASTURE'S SYNDROME	HEAVY-METAL POISONING
HYPERTENSION	lupus NEPHROPATHY
organic solvent exposure	POLYCYSTIC KIDNEY DISEASE
renal ARTERY ATHEROSCLEROSIS	RENAL CANCER

Symptoms and Diagnostic Path

Symptoms of renal failure depend on whether renal failure is acute or chronic. Acute renal failure typically causes neurologic symptoms. ANEMIA, hypertension (high blood pressure), congestive HEART FAILURE, and OSTEOPOROSIS (loss of BONE DENSITY and STRENGTH) often accompany chronic renal failure. The diagnostic path includes URINE and blood tests to assess kidney function, diagnostic imaging procedures such as ULTRASOUND and COMPUTED TOMOGRAPHY (CT) SCAN, and often kidney biopsy to microscopically examine the nephrons.

RENAL FAILURE SYMPTOMS

Acute Renal Failure	Chronic Renal Failure
edema	edema
gastrointestinal bleeding	fatigue
confusion	OLIGURIA (diminished URINE production)
loss of consciousness	headaches
seizures	NAUSEA, VOMITING, and loss of APPETITE

Treatment Options and Outlook

Treatment targets the underlying cause. Acute renal failure requires immediate and intensive medical care, often including hemodialysis. Dietary modifications (such as reduced sodium, protein, and fluid intake) and medications to control conditions such as diabetes and hypertension allow many people to live with chronic renal failure for years to decades. When chronic renal failure progresses to ESRD, renal dialysis or kidney transplantation become necessary to sustain life.

Chronic renal failure in children impairs growth because it interferes with the ability of the kidneys to maintain calcium balance within the body and to produce erythrocytes (red blood cells). Without adequate calcium the bones cannot grow, resulting in short stature. Erythrocytes are necessary to carry oxygen, GLUCOSE, and other NUTRIENTS to cells throughout the body. Without these nutrients, cells slow their rate of division. Doctors often prescribe calcitriol supplement, a form of vitamin D, for children who have chronic renal failure to improve the body's ability to retain calcium. Many doctors also prescribe HUMAN GROWTH HORMONE (HGH) SUPPLEMENT therapy to achieve normal growth patterns in children who have chronic renal failure, though not all doctors agree this is appropriate. Human growth HORMONE supplementation can have other deleterious effects on the body; it is important to balance such risks with the potential benefits.

Risk Factors and Preventive Measures

The major risk factors for chronic renal failure are diabetes and hypertension. Measures to reduce the risk for these conditions also lower the risk for kidney disease. Such measures include

- nutritious EATING HABITS
- daily physical activity
- SMOKING CESSATION
- maintenance of healthy body weight

Diligent control of diabetes or hypertension if these conditions are present can slow their effects on the kidneys. Because chronic renal failure tends to be progressive, it is important to address symptoms of deteriorating kidney function promptly and aggressively for optimal quality of life.

See also HEPATORENAL FAILURE; NEPHROTIC SYNDROME; NEPHRON.

renal tubular acidosis (RTA) A genetic disorder in which the renal tubule within the NEPHRON fails to release hydrogen ions into the filtrate. The consequence is a buildup of acid in the BLOOD (serum acidosis) that causes various symptoms and imbalances among the body's electrolytes. There are numerous forms of renal tubular acidosis (RTA), most of which are random (sporadic) though some types are familial. Common forms of RTA include

- type 1 RTA, which affects the distal tubule and may occur secondary to AUTOIMMUNE DISORDERS such as SJÖGREN'S SYNDROME or after KIDNEY TRANSPLANTATION
- type 2 RTA, which affects the proximal tubule and often accompanies conditions such as WILSON'S DISEASE, FANCONI'S SYNDROME, MULTIPLE MYELOMA, and HYPERPARATHYROIDISM as well as after kidney transplantation

- type 4 RTA, which may accompany NEPHROPATHY of DIABETES or HIV/AIDS, SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and SICKLE CELL DISEASE

The diagnostic path includes blood tests and URINE tests that measure acidity. Treatment is usually medication (pharmaceutical sodium bicarbonate) to maintain the blood's pH (acidity level) within the desired range and regular blood or urine tests to measure acidity.

See also GENETIC DISORDERS; GLOMERULUS; HYPERKALEMIA; INHERITANCE PATTERNS.

U

uremia A serious condition in which nitrogen-based toxins such as urea and creatinine, the primary waste products of METABOLISM, accumulate in the BLOOD because the KIDNEYS are unable to filter them out and pass them from the body via the URINE. Uremia indicates RENAL FAILURE. Urologists sometimes use the term azotemia to designate preclinical uremia—that is, rising levels of urea in the blood that have not yet reached a level at which they cause symptoms.

Symptoms of uremia include

- NAUSEA and VOMITING
- confusion
- HEADACHE
- loss of APPETITE
- lethargy and difficulty concentrating

Blood and urine tests to measure levels of blood urea nitrogen (BUN) and creatinine confirm the diagnosis. Treatment is generally RENAL DIALYSIS to filter metabolic wastes and toxins from the blood, to restore the body's electrolyte, chemical, and water balances. KIDNEY TRANSPLANTATION may be a viable treatment option when kidney failure becomes permanent, such as in END-STAGE RENAL DISEASE (ESRD).

See also NEPHROPATHY; NEPHROTOXINS.

ureter A tubular structure that carries URINE from the kidney to the BLADDER. Urine from the kidney's collecting tubules drains into the renal pelvis, which channels the urine into the ureter. The ureter exits the kidney at the hilus and parallels the inferior VENA CAVA (left ureter) or the AORTA (right ureter) through the abdomen to the pelvis. At the pelvis the ureter crosses over the respective iliac branches (ARTERY and VEIN) and enters the top back of the bladder. The ureter forms a short, flattened tunnel within the bladder wall before opening into the interior of the bladder. This tunnel functions as a valve to help keep urine from flowing back up the ureter from the bladder. Each ureter is about 12 inches long, though the left is slightly longer than the right as the left kidney sits about an inch higher in the abdomen. The structure of the ureters is the same in men and women.

A smooth epithelial membrane forms the inner lining of the ureter. Two layers of MUSCLE surround the ureteral epithelium, the first running more or less lengthwise (longitudinal) though spiraling widely around the epithelium, and the second wrapping around the ureter in a circular pattern. The outer layer of the ureter is fibrous tissue. The muscle layers of the ureter contract in rhythmic waves (PERISTALSIS) to move urine from the kidneys to the bladder. The ureter is fairly thick and rigid, with an inner diameter of only 3 or 4 millimeters.

For further discussion of the ureters within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also GLOMERULUS; KIDNEYS; NEPHRON; URETHRA; VESICOURETERAL REFLUX.

urethra A narrow, somewhat muscular tube that carries URINE from the BLADDER to the outside of the body. The point of exit is the urinary or urethral meatus. The urethral sphincter MUSCLE at the base of the bladder controls the release of urine into the urethra. Once the urethral sphincter relaxes to let urine pass, the urine flows to the outside of the body until the bladder empties and the urethral sphincter tightens. It may take a few seconds after the sphincter closes for the residual urine in the

urethra to make its way out the urethral opening. BLADDER CATHETERIZATION, CYSTOSCOPY, ureteroscopy, and intravesical therapies use the urethra to enter the urinary system (usually with sedation or ANESTHESIA, except catheterization).

In a woman the urethra is about an inch and a half long, extending from the base of the bladder to the external GENITALIA where it exits the body between the CLITORIS and the VAGINA. The urethra's only role in a woman is to carry urine from the body. In a man the urethra is about eight inches long and extends from the base of the bladder to exit the body at the tip of the PENIS. As it exits the bladder in a man the urethra passes through the PROSTATE GLAND, which encircles the neck of the bladder. The male urethra also carries SPERM during EJACULATION. The VAS DEFERENS, the tube that carries SEMEN from the male reproductive organs, enters the urethra at the prostate gland. A valve at the base of the urethra directs the flow of either urine or semen through the urethra.

For further discussion of the urethra within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also EPISPADIAS; HYPOSPADIAS; RETROGRADE EJACULATION.

urethral stricture Narrowing of the URETHRA, impeding the passage of URINE from the BLADDER to the outside of the body. Urethral stricture may be congenital (present at birth) or acquired such as through scarring resulting from repeated URETHRITIS, BLADDER CATHETERIZATION, and other irritations to the urethra. BENIGN PROSTATIC HYPERPLASIA (BPH) and PROSTATITIS also can cause urethral stricture in men.

Symptoms of urethral stricture include

- straining when urinating
- the sensation that the bladder does not empty with URINATION (URINARY RETENTION)
- diminished urine flow
- frequent URINARY TRACT INFECTION (UTI)

The diagnostic path begins with urinalysis to determine whether INFECTION is present. Further diagnostic procedures may include CYSTOSCOPY to examine the urethra and bladder, INTRAVENOUS PYELOGRAM (IVP) to assess the flow of BLOOD and urine through the urinary system, or COMPUTED TOMOGRAPHY (CT) SCAN or ULTRASOUND to visualize the structures of the lower pelvis. Treatment targets the identified cause and may include ANTIBIOTIC MEDICATIONS when infection is present in addition to other therapies. Such therapies often include cystoscopic surgery to cut away SCAR tissue within the urethra or open surgery (urethroplasty) to reconstruct a badly scarred or damaged urethra. These methods permanently restore the flow of urine through the urethra and have minimal complications or risks.

See also UROLITHIASIS.

urethritis INFLAMMATION of an URETER. INFECTION, typically a sexually transmitted disease (STD), is the most common cause of urethritis though urethritis may occur as a result of inflammation or irritation from trauma such as occurs with BLADDER CATHETERIZATION or CYSTOSCOPY. Traumatic urethritis improves rapidly when the source of the trauma is gone, often without further treatment. Urologists classify infectious urethritis as gonococcal urethritis (GU) or nongonococcal urethritis (NGU). Symptoms may be vague and transient (disappear in a few days) or nonexistent, though the infection remains. In about 40 percent of women, urethritis progresses to PELVIC INFLAMMATORY DISEASE (PID) and INFERTILITY. Repeated or untreated urethritis in men may destroy testicular tissue, resulting in sterility. As well, untreated urethritis in men or women remains contagious through sexual contact.

Symptoms and Diagnostic Path

Often urethritis does not have symptoms, particularly in women. When symptoms are present they typically include

- puslike or bloody discharge from the PENIS
- PAIN or burning with URINATION (DYSURIA)

Laboratory analysis of discharge or swabs of the interior of the urethra identify the responsible PATHOGEN. Generally no further diagnostic proce-

dures are necessary unless other health concerns coexist.

Treatment Options and Outlook

Treatment is the appropriate antibiotic medication to kill the pathogen. It is important to take the full amount of the antibiotic as prescribed. Though tempting to stop the medication when symptoms abate, incomplete treatment allows the BACTERIA to surge back to reinfect. It also can permit bacteria to develop resistance to commonly prescribed antibiotics, requiring more powerful antibiotics for subsequent treatment. Both GU and NGU can occur repeatedly when the person becomes reinfected. Each cycle of infection requires treatment. It is important (and in many states a legal requirement) to notify sexual partners so they also can receive treatment.

Risk Factors and Preventive Measures

The primary risk for GU and NGU infection is unprotected sex, particularly with multiple partners. Men who have sex with men are at highest risk. Safer sex methods, including the use of a new condom for each sex act, help reduce exposure to the bacteria that cause urethritis though are not foolproof. Traumatic urethritis sometimes becomes chronic in people who must use long-term bladder catheterization, such as those who have SPINAL CORD INJURY resulting in paraplegia. The urologist may prescribe prophylactic antibiotics and anti-inflammatory medications in such situations. Diligent PERSONAL HYGIENE further helps reduce irritation and infection.

See also CHLAMYDIA; CYSTITIS; EPIDIDYMITIS; GONORRHEA; PROSTATITIS; REITER'S SYNDROME; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASES (STDS).

urinary diversion A surgical procedure to create a method for the storage and passage of URINE from the body after cystectomy (surgical removal of the BLADDER). Though most often necessary following cystectomy to treat BLADDER CANCER or invasive cancer of the pelvic region, urinary diversion may be necessary after traumatic injury to the bladder. Urinary diversion may also be a palliative treatment for inoperable bladder or pelvic cancer, diverting the flow of urine to overcome urinary obstruction. Urinary diversion may be continent (collects and contains urine within the body), which most people prefer when it is possible, or incontinent (collects a steady flow of urine in a bag outside the body).

Continent Urinary Diversion

When the urethra remains intact the urologic surgeon can fashion a substitute bladder, called a neobladder, from a segment of bowel (which has the ability to expand somewhat), attaching the ureters and the URETHRA. The neobladder allows the person to urinate naturally. However, the neobladder requires more frequent, and usually timed or scheduled, emptying as it lacks the distention ability and capacity of the native bladder as well as the nerves that activate the micturition REFLEX.

When the cystectomy also includes removal of the urethra, the surgeon generally chooses to craft a collection reservoir from a segment of SMALL INTESTINE that remains in the abdominal cavity, then create a valved opening through the abdominal wall into the reservoir. The person periodically inserts a catheter into the opening to drain the urine, usually every three to four hours, including through the night. Though not as natural as the neobladder, the catheter reservoir still permits urinary continence.

Incontinent Urinary Diversion

Incontinent urinary diversion is similar to the catheter reservoir, except the opening through the abdominal wall, called a stoma, lacks a valve. The person attaches an ostomy bag over the opening using special adhesive. Urine drains continuously into the bag, and periodically the person removes the full bag and replaces it with a clean, empty bag. The bags are small and unobtrusive beneath the clothing. The adhesive ensures there is no leakage of urine. A urostomy bag may require changing every six to eight hours. Surgeons use this method, called urostomy or ileal conduit, primarily when continent urinary diversion is not a viable option.

Outlook and Lifestyle Modifications

Urinary diversion requires diligent attention to hygiene and emptying collected urine. Though the neobladder is the most natural urinary diversion

method, it requires more frequent emptying than would the natural bladder. Likewise the catheter reservoir, which further requires the person to carry a catheter at all times. URINARY TRACT INFECTION (UTI) tend to be more frequent in people who have any form of urinary diversion, though are most common with urostomy. Urostomy also may cause irritation to the SKIN around the stoma. Many people who have urostomies or catheter reservoirs feel self-conscious about them. The urologist or hospital can provide information about support groups where people who have urinary diversions can share their concerns and experiences.

See also COLOSTOMY; ILEOANAL RESERVOIR; ILEOSTOMY; QUALITY OF LIFE; SURGERY BENEFIT AND RISK ASSESSMENT.

urinary frequency The need to urinate more often than normal. Urinary frequency is common in PREGNANCY, CYSTITIS, URINARY TRACT INFECTION (UTI), BENIGN PROSTATIC HYPERPLASIA (BPH) and PROSTATITIS in men, and DIABETES. Urinary frequency at night is NOCTURIA. Sometimes the cause is excessive fluid consumption, particularly in the evening when nocturia is a problem. The diagnostic path may include urinalysis, assessment of any symptoms that accompany the urinary frequency, and procedures such as abdominal ULTRASOUND or CYSTOSCOPY to evaluate the BLADDER and URETHRA. Treatment targets the underlying cause. The doctor may prescribe medications such as tolterodine or oxybutynin to slow the bladder's response when no clear-cut cause emerges and symptoms persist.

See also URINARY INCONTINENCE; URINARY URGENCY.

urinary incontinence The involuntary leakage of URINE from the URETHRA. Health experts estimate that as many as 12 million Americans experience some degree of urinary incontinence, which becomes increasingly common with advancing age. There are several types of urinary continence. They include

- stress incontinence, in which urine leaks with activities such as sneezing, coughing, or laughing
- urge incontinence, in which urine leakage accompanies a sudden and overwhelming desire to urinate
- overflow incontinence, in which the bladder fails to send or respond to the normal NERVE signals that direct urination and becomes overly full, eventually leaking urine because it can hold no more volume

Many people, particularly women past MENOPAUSE, experience a combination of stress and urge incontinence. This combination form of urinary incontinence develops when the pelvic muscles and ligaments that support the bladder weaken and stretch. Overflow incontinence is more common in older men who have BENIGN PROSTATIC HYPERPLASIA (BPH). The enlarged PROSTATE GLAND can constrict the urethra, preventing urine from leaving the bladder. Overflow incontinence may also develop in people who have NEUROPATHY of DIABETES, long-standing chronic ALCOHOLISM, or conditions of the NERVOUS SYSTEM that affect control of involuntary functions such as MULTIPLE SCLEROSIS.

The diagnostic path includes a careful history of the urinary incontinence, BLOOD and urine tests, and possibly diagnostic imaging procedures such as ULTRASOUND or CYSTOSCOPY to identify any underlying conditions that could be causing the urinary incontinence. Treatment may be lifestyle modification, such as altering fluid consumption habits or emptying the bladder on a schedule. Many people, especially women, regain continence with KEGEL EXERCISES to strengthen and tone the pubococcygeal MUSCLE that forms the pelvic floor. Incontinence pads and other items help protect clothing from leaking urine. Sometimes medications to slow the bladder's response, such as oxybutynin (Ditropan), help ease urge incontinence. In situations that do not improve the urologist may suggest surgery to tighten pelvic muscles or the urethral sphincter. Though finding the most effective solution may take time, most people are able to successfully manage urinary incontinence.

See also ENURESIS.

urinary retention The inability to completely empty URINE from the BLADDER with URINATION. Because urinary retention presents a risk for bacterial URINARY TRACT INFECTION (UTI) or NEPHRITIS (INFECTION of the KIDNEYS), it is important to find and treat its cause. The most common cause is an

obstruction that blocks or narrows the URETHRA such as a bladder stone (UROLITHIASIS), URETHRITIS or URETHRAL STRICTURE, BENIGN PROSTATIC HYPERPLASIA (BPH) or PROSTATITIS in men, CYSTOCELE (sagging of the bladder) or UTERINE PROLAPSE in women, and rarely a tumor. As well, STROKE, SPINAL CORD INJURY, or TRAUMATIC BRAIN INJURY (TBI) can damage the nerves that control urination. The diagnostic path may include urinalysis and CYSTOSCOPY or ULTRASOUND to evaluate the urethra and bladder. Treatment targets the underlying cause and may include BLADDER CATHETERIZATION to empty the bladder of urine, either as an emergency procedure for acute urinary retention or on a routine basis for chronic urinary retention. Often, the underlying cause is treatable and the urinary retention resolves.

See also URINARY FREQUENCY; URINARY URGENCY.

urinary urgency The overwhelming sensation of the need to urinate. Urinary urgency, also called overactive BLADDER, can cause a person to urinate dozens of times each day. Though a common symptom of conditions such as CYSTITIS and URINARY TRACT INFECTION (UTI), especially when urinary urgency occurs in combination with URINARY FREQUENCY, urinary urgency may indicate a blockage in the urinary tract or result from neurologic conditions or injuries. Urinary urgency may also result in URINARY INCONTINENCE (inability to hold the URINE), even when the amount of urine in the bladder is small. Other common causes include DIABETES, PREGNANCY in women and BENIGN PROSTATIC HYPERPLASIA (BPH) in men. The diagnostic path begins with an assessment of any symptoms that accompany the urinary urgency, urinalysis, and perhaps procedures such as CYSTOSCOPY and pelvic ULTRASOUND to examine the bladder and URETHRA. Treatment targets any identified underlying cause. The doctor may prescribe medications such as tolterodine or oxybutynin to slow the bladder's response.

See also NEUROGENIC BLADDER; URINARY RETENTION.

urinary tract infection (UTI) A bacterial INFECTION of the BLADDER and URETHRA. The most common bacterial culprit is *Escherichia coli*, which is normally present in the gastrointestinal tract. Other BACTERIA may also cause UTI. Typically UTI, commonly called bladder infection, refers to infection that remains in the bladder and urethra. UTI may be acute (come on suddenly) or chronic (occur repeatedly over time). Untreated or undertreated UTI can spread into the KIDNEYS (NEPHRITIS), causing significant illness and the potential for permanent damage to the delicate tubules and glomeruli of the nephrons.

Symptoms and Diagnostic Path

Symptoms of acute UTI tend to be more intense than symptoms of chronic UTI, though either can be highly uncomfortable. The general symptoms of UTI include

- DYSURIA (burning with URINATION)
- URINARY FREQUENCY and URINARY URGENCY
- HEMATURIA (bloody URINE)
- cloudy, foul-smelling urine
- aching or discomfort in the lower pelvis or lower back

Urinalysis shows the presence of bacteria in most UTIs, confirming the diagnosis. Urinalysis does not identify the kind of bacteria, however. The doctor may choose to obtain a urine sample via BLADDER CATHETERIZATION (to avoid contamination by bacteria normally on the SKIN's surface) and culture it in the laboratory to determine the kind of bacteria present. A urine culture is especially helpful in chronic UTI or when symptoms fail to respond to initial treatment. A urologist may recommend additional diagnostic procedures for chronic UTI to determine the underlying reasons for the frequency or persistence of infection.

Treatment Options and Outlook

ANTIBIOTIC MEDICATIONS are the standard treatment for UTI. The antibiotic and length of treatment depend on the bacteria causing the infection. Most UTIs in women respond to a 3-day course of the antibiotic TMP-SMX or an antibiotic in the fluoroquinolone family such as ciprofloxacin. Women who cannot take either of these antibiotics may instead take an antibiotic in the tetracycline family (tetracycline or doxycycline) or the cephalosporin family (such as cefaclor). Men take the same antibiotics though often require a longer course,

typically 7 to 10 days. It is important to continue taking all prescribed doses of the antibiotic, even when symptoms improve, to make sure the antibiotic kills all the bacteria. The doctor may prescribe low-DOSE antibiotic medications for long-term preventive therapy (six months to a year) in women who have recurrent UTIs.

The medication phenazopyridine, a topical anesthetic that numbs the inner lining of the bladder and urethra, relieves discomfort during the first 36 to 48 hours of the UTI until the antibiotic begins eliminating bacteria. Phenazopyridine colors the urine deep orange and stains clothing. Some people experience intense bladder spasms, for which the doctor may prescribe a short course of antispasmodic medications such as flavoxate or methenamine.

ANTIBIOTICS COMMONLY PRESCRIBED TO TREAT UTI

amoxicillin	cefaclor	cefixime
cefotaxime	cefpodoxime	cefprozil
cefuroxime axetil	ciprofloxacin	doxycycline
fosfomycin	levofloxacin	nitrofurantoin
norfloxacin	ofloxacin	sparfloxacin
sulfamethoxazole trimethoprim	tetracycline	TMP-SMX

Risk Factors and Preventive Measures

UTIs are common in girls and women though uncommon in boys and men because of differences in anatomy. The very short female urethra provides an easy route for bacteria to travel into the bladder. Health experts estimate that one in five women will have at least one UTI during her lifetime. Measures to reduce the risk for UTI include

- drinking enough water (six to eight 8-ounce glasses daily)
- urinating when the bladder signals it is full
- wiping with toilet tissue from front to back
- urinating soon after SEXUAL INTERCOURSE
- prophylactic antibiotics when UTI occurs three times in a year or more frequently

About 20 percent of women who have one UTI have another; recurrent UTI is rare in men. Though untreated or undertreated UTI can cause serious and permanent damage to the urinary system, people who have appropriately treated UTIs typically recover completely and without residual complications.

See also CYSTITIS; GLOMERULUS; NEPHRON; SEXUALLY TRANSMITTED DISEASES (STDS); URETHRITIS.

urination The act of passing URINE from the BLADDER, also called uresis or micturition. Urination occurs when the urethral sphincter relaxes at the same time the detrusor MUSCLE that forms the middle layer of the bladder wall contracts, squeezing urine into the URETHRA. The urethra carries the urine to the meatus, its opening on the outer surface of the body. In men the meatus is at the tip of the PENIS; in women the meatus is within the VULVA between the CLITORIS and the VAGINA. Urination ends when the bladder sphincter closes and the residual urine in the urethra passes from the body.

Urination is a blend of involuntary and voluntary control. At birth urination is completely under the control of the micturition REFLEX and the sympathetic NERVOUS SYSTEM, which regulates involuntary functions. The micturition reflex is the series of events that begins when the filling of the bladder with urine activates specialized nerves in the bladder wall called stretch receptors. The stretch receptors send NERVE signals out to the SPINAL NERVES (S2, S3, and S4) that control the urethral sphincter and the detrusor muscle. The spinal nerves send back the nerve signals that stimulate the detrusor muscle to contract and the urethral sphincter to relax. A structure within the pons of the brainstem, the pontine micturition center (PMC), coordinates these functions to occur simultaneously.

The ability to control urination becomes possible around the ages of three to five when the muscles and nerve paths mature. At this point of development the BRAIN can override the involuntary nerve processes and the pubococcygeal muscle, which is a voluntary muscle, can override the involuntary muscle functions of the bladder. The normal frequency of urination varies among individuals and with fluid consumption, which largely determines urine volume. A healthy adult produces between 1.5 and 3 liters of urine every 24 hours. Typically the stretch receptors respond when the bladder contains about 200 to 300 milli-

liters of urine; maximum capacity of the bladder is about 500 ml.

CONDITIONS OF ALTERED URINATION

ANURIA	DYSURIA
HEMATURIA	NOCTURIA
URINARY FREQUENCY	URINARY INCONTINENCE
URINARY RETENTION	URINARY URGENCY

See also NEUROGENIC BLADDER.

urine The liquid the KIDNEYS generate to pass wastes and excess fluid from the body. The typical adult makes and passes between 1,500 and 3,000 milliliters (1.5 to 3 liters) of urine every 24 hours. Numerous variables influence the volume and composition or urine, though in general urine is 95 percent water and 5 percent suspended or dissolved solids.

Most of the solids urine contains are organic wastes in the forms of urea, uric acid, creatinine, and ammonia. These are the nitrogen-based waste byproducts of METABOLISM that the kidneys filter from the BLOOD. The urine also contains minerals (electrolytes) the kidneys excrete to maintain the body's electrolyte and fluid balance. Excreted electrolytes include sodium, potassium, chloride, magnesium, phosphate, and calcium. Normal urine may contain small amounts of ALBUMIN (protein).

Urine of normal concentration is pale yellow and has no odor. Dilute urine is colorless; concentrated urine can appear dark yellow to orange. Dietary substances, certain medications, and certain health conditions can alter the color as well as the odor of the urine. Normal urine is slightly acidic and has a specific gravity of 1.010 to 1.025, slightly above that of water. Deviations from normal urine composition and concentration suggest various health conditions and may require diagnostic evaluation.

For further discussion of the urine within the context of the urinary system's structure and function please see the overview section "The Urinary System."

See also ALBUMINURIA; ANURIA; CYSTINURIA; HEMATURIA; OLIGURIA; UREMIA; UROLITHIASIS.

urolithiasis The formation of calcifications (also called calculi) in the BLADDER. Most bladder stones, like kidney stones, form of calcium in combination with oxalate (the most common combination), phosphate, or magnesium. Bladder stones are less common today than kidney stones (NEPHROLITHIASIS), though throughout recorded history bladder stones have been a common urologic condition. Bladder stones are most likely to form when URINE remains in the bladder for an extended time, particularly with URINARY RETENTION (in which the bladder fails to completely empty with URINATION). URETHRAL STRICTURE, CYSTOCELE, BENIGN PROSTATIC HYPERPLASIA (BPH), long-term BLADDER CATHETERIZATION, and NEUROGENIC BLADDER are among the conditions that contribute to the formation of bladder stones. Chronic DEHYDRATION, such as occurs with drinking too little water, further contributes to calcification. Bladder stones are also common during PREGNANCY.

In urinary stasis the minerals dissolved in the urine begin to settle out when the urine is static (not moving), forming crystals. The formed crystals attract more of their composite minerals, eventually hardening into calculi. Small stones often easily pass through the urethra in the urine without the person's awareness of them. Stones that are large enough to scrape the walls of the urethra, or sandlike clumps of calculi that surge through the URETHRA, may cause irritation such as DYSURIA (burning sensation) with urination. Other symptoms may include URINARY FREQUENCY, URINARY URGENCY, and urinary hesitation (difficulty starting urination, or start-and-stop urination).

A stone that completely blocks the urethra, often at the neck of the bladder, causes excruciating PAIN that may feel as though it arises in the groin or, in men, in the TESTES (testicles). Often a change in position relieves the pain, causing the urine to wash the stone from its point of occlusion. A stone that is larger than the diameter of the urethra will intermittently though persistently obstruct the passage of urine. It may also cause bleeding, resulting in HEMATURIA (blood in the urine).

The diagnostic path typically includes urinalysis, ULTRASOUND to detect the presence of stones in the bladder, and CYSTOSCOPY. Cystoscopy often is both diagnostic and therapeutic, allowing the urologist to confirm the presence of stones as well as remove them from the bladder. Larger stones may require treatments such as EXTRACORPOREAL SHOCKWAVE

LITHOTRIPSY (ESWL) or surgical procedures such as percutaneous lithotomy or open cystostomy to remove the stones. Most people recover fully. Bladder stones tend to recur, however.

See also CYSTINURIA; HYPERCALCIURIA; HYPEROXALURIA.

urostomy See URINARY DIVERSION.

V

vesicoureteral reflux A condition in which URINE backflows from the BLADDER into the ureters toward the KIDNEYS. Vesicoureteral reflux may result from congenital anomalies in the structure of the ureters, such as short ureters or ureters that enter the bladder wall in an unusual location or at an unusual angle. Normally the URETER forms a short, flattened tunnel within the bladder wall that functions like a valve to keep urine from reentering the ureter from the bladder. Structural anomalies may prevent the valvelike action of the ureter's entrance into the bladder from functioning properly, such that when the bladder fills with urine the ureter is open and allows urine to enter.

Vesicoureteral reflux may also develop secondary to an obstruction that blocks the flow of urine from the bladder, such as bladder stones (UROLITHIASIS) or an enlarged PROSTATE GLAND in a man. Such an obstruction causes the bladder to overdistend, which causes the ureteral tunnels to open and allow urine to enter the ureters. INFECTION that inflames and narrows the URETHRA also can obstruct the flow of urine out of the bladder. Vesicoureteral reflux presents a high risk for INFLAMMATION and bacterial infection of the kidneys

VESICOURETERAL REFLUX GRADING

Reflux Grade	Extent of Urine Reflux	Effect on Kidneys
grade 1	part way up URETER but not into the kidney	increased risk for NEPHRITIS
grade 2	completely up ureter to renal pelvis	increased risk for nephritis
grade 3	URINE backs up into the renal pelvis and renal calyces	mild dilation of renal pelvis and ureters mild nephritis likely
grade 4	urine distends the renal pelvis and renal calyces	significant dilation of ureters nephritis HYDRONEPHROSIS with mild to moderate impaired renal function risk of permanent kidney damage
grade 5	as much or more urine refluxes as passes from the URETHRA	extensive and persistent dilation of ureters, renal pelvis, and renal calyces nephritis hydronephrosis with significant impaired renal function secondary problems such as HYPERTENSION permanent kidney damage likely

(NEPHRITIS) by introducing into the kidneys BACTERIA that may be present in the urine. Vesicoureteral reflux also can cause HYDRONEPHROSIS, dilation of the renal pelvis that results from the accumulation of urine. Nephritis and hydronephrosis both can cause permanent and sometimes progressive kidney damage.

Symptoms and Diagnostic Path

The most common indication of vesicoureteral reflux is infection, the symptoms of which typically include

- flank or ABDOMINAL PAIN
- FEVER and chills
- HEMATURIA (BLOOD in the urine) or cloudy urine
- DYSURIA (discomfort with URINATION)
- urinary frequency and urinary urgency

As well, the person may strain when urinating and feel as though urine remains in the bladder (URINARY RETENTION) after urinating. The diagnostic path begins with urinalysis, which shows the presence of bacteria, leukocytes (white blood cells that fight infection), and erythrocytes (red blood cells) when there is an infection. The urologist may perform diagnostic imaging procedures, such as abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, to visualize the structures of the urinary system and identify any anomalies. Radionuclide scan, INTRAVENOUS PYELOGRAM (IVP), and voiding CYSTOURETHROGRAM are additional diagnostic procedures that help the urologist assess the urinary system's structure and function. Diagnosis of vesicoureteral reflux includes the designation of grade, which denotes the severity of the urine reflux and the effect on the kidneys.

Treatment Options and Outlook

Infection requires immediate treatment with ANTIBIOTIC MEDICATIONS. When the vesicoureteral reflux occurs secondary to an obstructive condition, treatment targets the underlying cause as well as any consequential infection. Treatment for primary vesicoureteral reflux depends on the person's age and the grade of the reflux. Children are likely to outgrow grade 1 and grade 2 reflux when the cause is short ureters and often when the cause is unusual entry of the ureters into the bladder. Grade 3 reflux may require corrective surgery. Grade 4 and grade 5 refluxes require reconstructive surgery such as ureteroneocystostomy, in which the surgeon creates new insertion tunnels into the bladder for the ureters. Appropriate treatment reduces the risk for permanent damage to the kidneys and restores the normal flow of urine.

Risk Factors and Preventive Measures

In children the primary risk factors for vesicoureteral reflux are anomalies of structure within the urinary system; these are not preventable. In adults risk factors for vesicoureteral reflux include NEPHROLITHIASIS (kidney stones), urolithiasis, chronic URINARY TRACT INFECTION (UTI), and BENIGN PROSTATIC HYPERPLASIA (BPH) in men. Prompt and appropriate treatment for these conditions reduces the risk they will cause vesicoureteral reflux.

See also BLADDER EXSTROPHY; CONGENITAL ANOMALY; SURGERY BENEFIT AND RISK ASSESSMENT.

Wilms's tumor A malignant (cancerous) growth in the kidney. Wilms's tumor, also called nephroblastoma, nearly always affects children under age six. Though relatively rare, with doctors diagnosing about 500 children a year in the United States with this form of kidney cancer, Wilms's tumor is the most common cancer of the kidney that occurs in children. Current treatment approaches have much improved survival, with the five-year survival rate now exceeding 90 percent.

Symptoms and Diagnostic Path

Wilms's tumor may not show symptoms until it is quite large, at which point a parent or caregiver may see or feel the tumor as a lump in the child's belly. The pediatrician may discover Wilms's tumor during a routine well-child examination. When the tumor causes symptoms, they often include

- HEMATURIA (bloody URINE)

STAGING OF WILMS'S TUMOR

Wilms's Tumor Stage	Extent of Cancer	Treatment Protocols/Options
stage 1	tumor is small and remains localized in one kidney	partial or simple NEPHRECTOMY followed by CHEMOTHERAPY
stage 2	tumor extends beyond the kidney though remains confined to a single mass that surgery can completely remove	radical nephrectomy followed by chemotherapy
stage 3	tumor extends to adjacent structures and lymph nodes and surgery cannot completely remove it	chemotherapy before surgery radical nephrectomy followed by chemotherapy and possibly RADIATION THERAPY
stage 4	tumor has metastasized to distant sites	chemotherapy nephrectomy radiation therapy
stage 5	both KIDNEYS have tumors	partial nephrectomy of both kidneys to remove as much cancer as possible yet retain kidney function chemotherapy repeat partial nephrectomy radiation therapy
inoperable	tumor is very large or located too close to vital BLOOD vessels for surgery to be viable	chemotherapy, radiation therapy, or a combination to reduce the tumor's size

- decreased APPETITE and weight loss
- NAUSEA and VOMITING
- abdominal discomfort or PAIN
- generalized irritability and crankiness

The diagnostic path begins with a comprehensive physical examination, BLOOD tests, and urinalysis. Diagnostic imaging procedures such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI) can identify the presence, size, and location of the tumor. Biopsy of the tumor is necessary to confirm the diagnosis.

Microscopic examination of the biopsied tissue further allows the pathologist to determine whether the tumor's cells are anaplastic, which means they are highly irregular and divide both rapidly and erratically. Tumors of anaplastic cells may be diffuse through the kidney and are more difficult to treat than tumors of what pathologists call favorable cells (cancerous cells that are more pathologically normal). The pathologist also assigns the cancer a grade that identifies the extent to which the tumor has spread (metastasized), which helps determine the appropriate treatment options.

Treatment Options and Outlook

NEPHRECTOMY (surgery to remove the affected kidney) in combination with CHEMOTHERAPY is the standard treatment for Wilms's tumor cancers. Partial nephrectomy removes the tumor and a margin of kidney tissue around it; simple nephrectomy removes the entire kidney. Radical nephrectomy removes the kidney. The oncologist may also add RADIATION THERAPY when the cancer's stage is advanced or its cells are anaplastic regardless of stage.

When the tumor is very large or the cancer involves both KIDNEYS, the oncologist may recommend chemotherapy or radiation therapy (or a combination of both) before surgery to shrink the tumors as much as possible. The oncologist may suggest participation in a clinical trial for inoperable, stage 5, or recurrent Wilms's tumor.

Treatment success largely correlates to the stage of the Wilms's tumor (the size of the tumor and the extent to which it has metastasized) and the characteristics of the cancer cells (anaplastic or favorable) at the time of diagnosis. Wilms's tumor is among the childhood cancers doctors consider curable.

Risk Factors and Preventive Measures

Researchers have recently identified GENE mutations that account about 30 percent of Wilms's tumor cancers. Located on CHROMOSOME 11, these are the Wilms's tumor 1 (WT1) and 2 (WT2) genes and provide encoding for development of urinary and genital structures. Wilms's tumor also is associated with several rare genetic syndromes, making it likely that other gene mutations further contribute to the errant encoding that allows these primitive cells to thrive. Family history raises the risk for Wilms's tumor, as it appears the gene mutations are sometimes hereditary.

Researchers believe Wilms's tumor represents clusters of cells in the kidneys that remain primitive, a consequence of the WT1 and WT2 mutations. When these primitive cells divide, they continue to do so at the same rapid rate of cell division that was normal in the EMBRYO. In the older child's body, however, this is inappropriate and the cells grow out of control, some wildly (the anaplastic cells). Some researchers believe the cell growth continues from early developmental stages and ultimately manifests as a tumor when the cluster of cells achieves enough mass. Other researchers believe environmental factors, perhaps processes in the body related to growth, trigger the cells to resume dividing.

There are no measures to prevent Wilms's tumor. Families who have had children with Wilms's tumor should have any other children undergo regular routine medical examinations that include screening (such as ultrasound) for the cancer. Doctors do not yet know the long-term health implications for Wilms's tumor survivors as the treatments that make survival possible have not been available long enough for many survivors to have yet reached adulthood.

See also BLADDER CANCER; CANCER TREATMENT OPTIONS AND DECISIONS; MUTATION; RENAL CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

THE REPRODUCTIVE SYSTEM

The organs and functions of the reproductive system make possible the creation of new life. Physician specialists who treat health conditions of the male reproductive system are urologists. Physician specialists who treat health conditions of the female reproductive system are gynecologists. Health-care providers who provide care during PREGNANCY and CHILDBIRTH are obstetricians (physician specialists) and midwives (usually registered nurses). Nurse practitioners (registered nurses with advanced specialized training and credentials) often function as women's health-care specialists, providing routine wellness care and treatment for minor reproductive and SEXUAL HEALTH conditions.

This section, "The Reproductive System," presents a discussion of the organs and structures of the male and female reproductive systems, an overview of reproductive and sexual health and disorders, and entries about the health conditions that involve the male and female reproductive systems. "The Urinary System" contains entries about male organs and structures that share urinary and reproductive functions. "Genetics and Molecular Medicine" contains entries about the genetics of reproduction. "The Endocrine System" contains entries about the sex hormones.

Structures of the Female Reproductive System

BREAST
- nipple
- areola
- lactiferous glands
- lactiferous ducts

OVARIES

ovum

FALLOPIAN TUBES
- fimbriae

UTERUS

CERVIX

VAGINA
- Bartholin's glands
- hymen

labia

CLITORIS

Structures of the Male Reproductive System

PENIS
- foreskin
- glans
- meatus

URETHRA
- corpora cavernosa
- corpus spongiosum

SCROTUM

TESTICLES

SPERM
- epididymis

VAS DEFERENS

PROSTATE GLAND
- seminal vesicle
- urethra

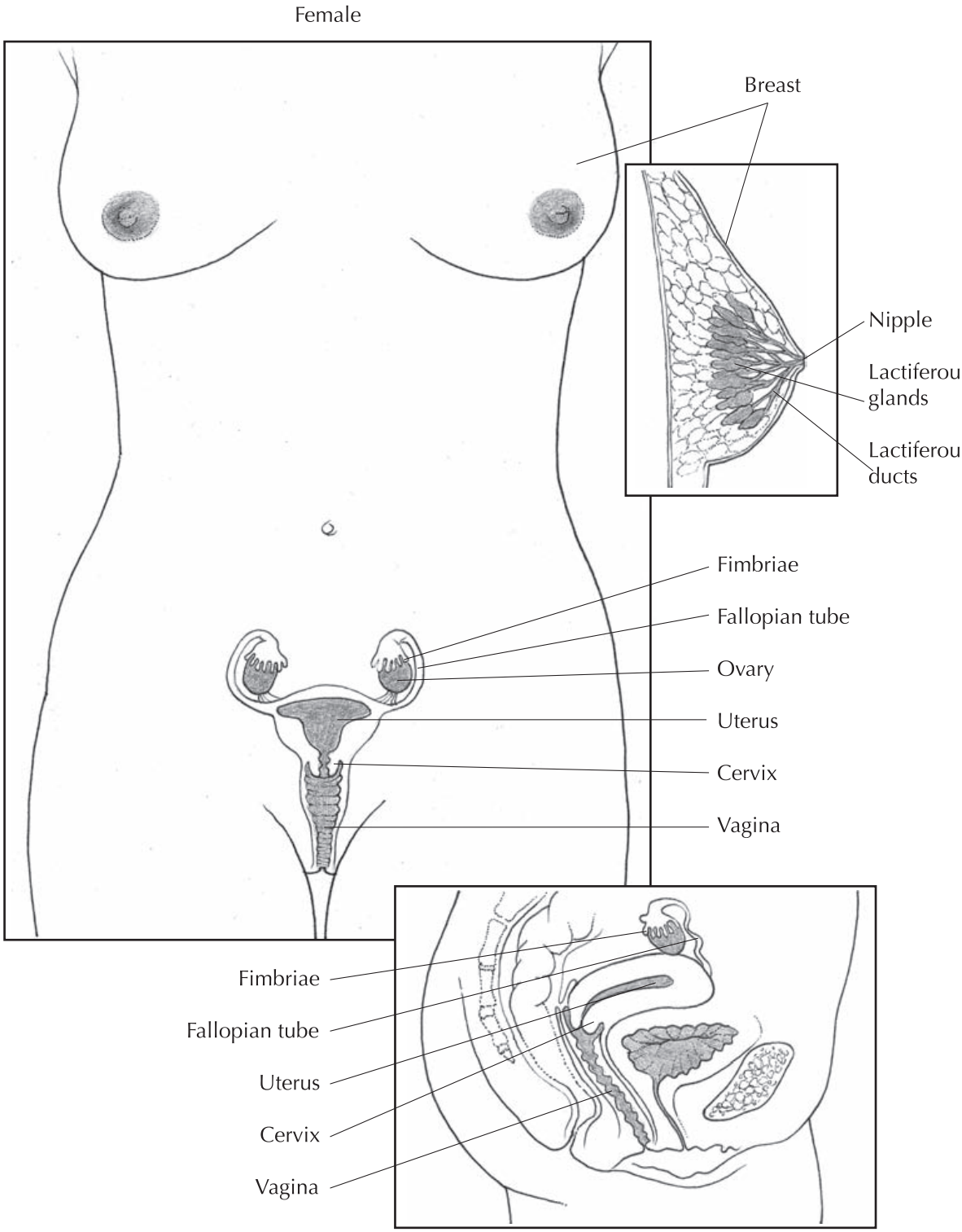
Functions of the Reproductive System

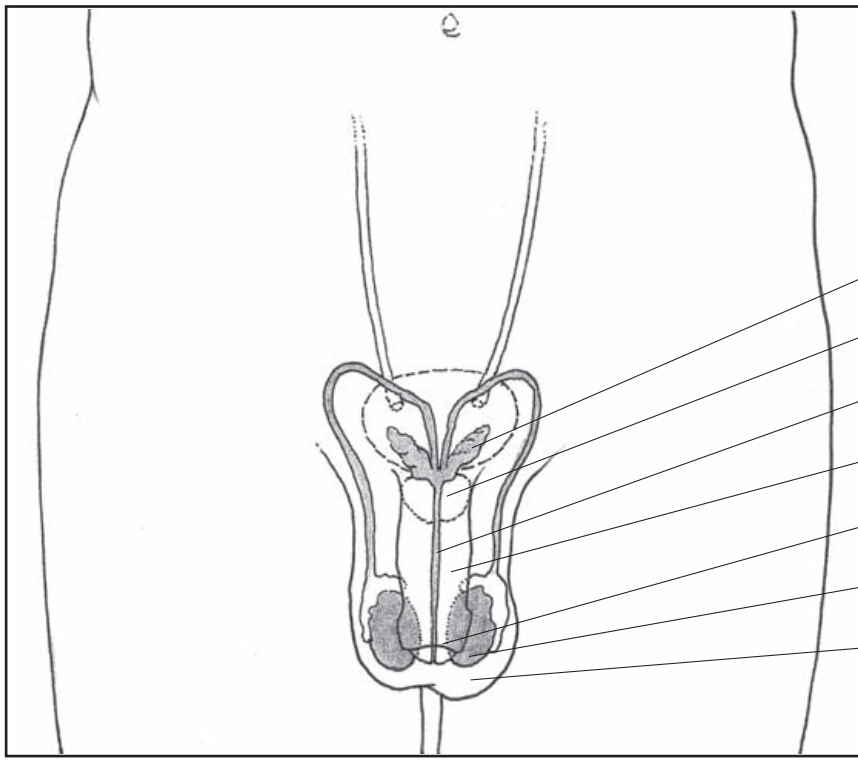
Human reproduction requires participation from both male and female, each of which contributes one half the genetic material necessary for human existence. The cells that carry this material are the gametes—the OVA, or eggs, from the female half and the spermatozoa, or SPERM, from the male half. Determining gender are the sex chromosomes, one from each gamete to form the pair that designates the gender of the new life. Though gender distinction is apparent at birth, functional characteristics of gender do not emerge until late childhood when hormonal shifts initiate the changes of PUBERTY. At puberty the levels of androgens and estrogens increase in the body, initiating the emergence of the secondary sexual characteristics that mark reproductive maturity.

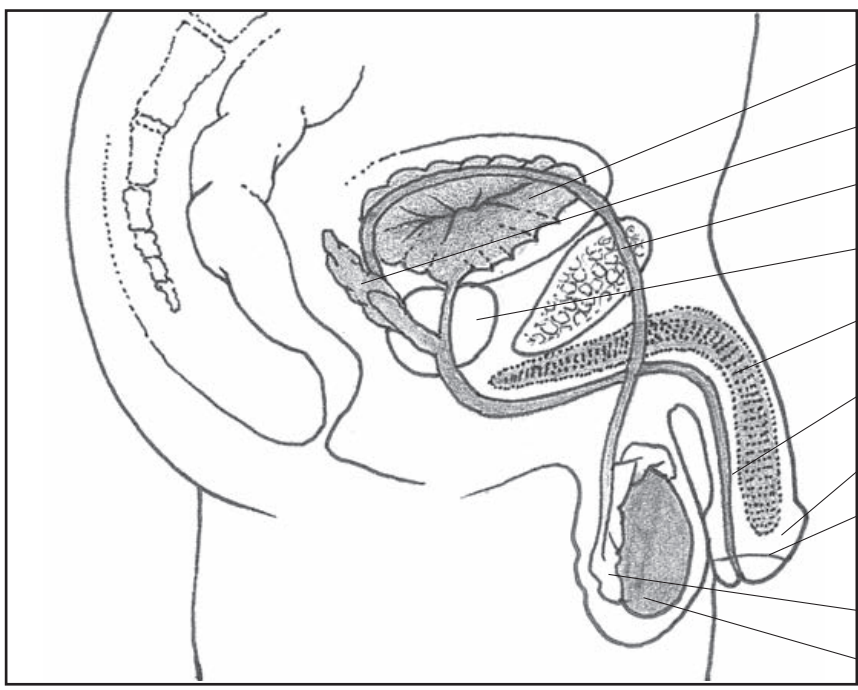
From a common beginning: embryonic gender differentiation The glands that both represent and sustain gender are the gonads—the OVARIES in the woman and TESTICLES, or testes, in the man. In the embryo these structures arise from the same base cells in the mesoderm (the middle layer of germ cells in the embryo) called the gonadal ridge. Until seven weeks, the embryo is androgynous (has no gender characteristics; male and female appear the same) with rudimentary structures—the genital tubercle, labioscrotal swellings, and urogenital groove and folds—that will evolve into gender-appropriate organs as the embryo develops.

At seven weeks the gonadal ridge organizes into a two-layer structure. If the genetic composi-

The Female Reproductive System




Seminal vesicle
Prostate gland
Urethra
Penis
Foreskin
Testicle
Scrotum


Bladder
Seminal vesicle
Vas deferens
Prostate gland
Corpus cavernosum
Urethra
Penis
Foreskin
Epididymis
Testicle

tion of the embryo is male, the gonadal ridge begins to produce TESTOSTERONE and a hormone unique to embryonic development, müllerian-inhibiting hormone. In response to testosterone the inner layer, the medulla, begins to take shape as the testes and the outer layer, the cortex, degenerates. The genital tubercle becomes the glans PENIS, the urogenital groove and folds enlarge to form the rest of the penis, and the labioscrotal swellings fuse to form the SCROTUM.

If the embryo's genetic composition is female there is no secretion of testosterone and müllerian-inhibiting hormone. So instead the outer layer, the cortex, begins to develop into the ovaries and the medulla deteriorates. The genital tubercle becomes the CLITORIS, the urogenital groove and folds become the VAGINA and labia minora, and the labioscrotal swellings form the labia majora. Primordial germ cells from the yolk sac migrate into the evolving testes or ovaries to become gametes (ova or sperm) as development continues. By 12 weeks gender differentiation is complete, though gender does not become detectable with ULTRASOUND imaging until the 20th week or later.

THE MYTHOLOGY OF THE HYMEN

The hymen, a narrow ring of membranous tissue that extends across the opening of the VAGINA, derives from the Greek god of the wedding feast, Hymen (also Hymenaeus). Hymen was the progeny of Dionysus, the god of FERTILITY, and Aphrodite, the goddess of love. Though the belief persists today that an intact hymen is evidence of a woman's virginity, in truth numerous activities (tampon use, horseback riding, bicycling, and gymnastics to name a few) can rupture the hymen. As well, the structure of the hymen varies widely among women and may be so insignificant as to not impede the penetration of the erect PENIS.

Transition to fertility: puberty Despite genital differences, boys and girls are fairly much alike physiologically for a dozen years or so after birth. Then hormonal signals trigger the onset of puberty, the transition from childhood to sexual and reproductive maturity. Though researchers do not know what activates the hormonal signals, the consequences are very familiar: the emergence of SECONDARY SEXUAL CHARACTERISTICS. The ovaries and testicles again become active, initiating the anatomic and physiologic changes that transform boys to men and girls to women. With sexual and reproductive maturity complete, SEXUAL INTERCOURSE and pregnancy become possible.

New life: conception, pregnancy, and childbirth On the surface of it, reproduction is an astonishingly simple premise, and its organs uniquely suited to its purpose. During sexual intercourse the erect penis fits precisely within the vagina, reaching to the CERVIX. EJACULATION deposits millions of sperm in the upper vagina, a short swim from the cervical os (opening through the cervix into the UTERUS). When conditions and timing are right, the sperm make their way through the cervix and uterus and into one of the FALLOPIAN TUBES, encounter the ovum (egg), and one of the millions penetrates the ovum to fertilize it. The resulting ZYGOTE travels down the fallopian tube, tumbles into the uterus, and implants itself into the dense, spongy endometrium: CONCEPTION.

The woman's body nourishes and shelters the developing FETUS, expanding and changing to accommodate its needs. The uterus stretches up to 10 times its normal size, pushing the abdominal wall outward. Again it is hormones that facilitate and support these processes, and hormones that bring the pregnancy to its conclusion: childbirth.

In the process of it, of course, there is nothing simple about any dimension of reproduction. Reproduction represents one of the most intricately choreographed experiences the human body can accommodate. Hundreds of hormones direct countless interactions, each of which spurs other events. Numerous factors, internal and external, influence reproduction to make it possible or not possible. Among the most significant advances in reproductive medicine are technologies to assist the process at various points along the reproductive continuum, from fertilization through childbirth.

Completing the cycle: menopause Men remain fertile nearly the rest of their lives after puberty, though sperm production and quality tend to diminish in later life as testosterone levels decrease. FERTILITY ends for women with MENOPAUSE, the cessation of OVULATION and men-

strual cycles. The ovaries contain a finite number of ova, present at birth. From the onset of MENSTRUATION to midlife, each monthly cycle causes a half dozen to a dozen ovarian follicles to ripen. Usually only one ovum (egg) reaches full maturity and leaves the ovary; the others atrophy (shrink) and the ovary reabsorbs them. By midlife the ovaries have made it pretty much through their supply of ova, far fewer follicles activate with each MENSTRUAL CYCLE, and ovarian function begins to shut down. Over a period of five to eight years, menstrual cycles become irregular and eventually infrequent until they stop altogether.

Health and Disorders of the Reproductive System

The health of the reproductive system, male or female, experiences internal and external influences. Internally the reproductive system relies significantly on an intricate hormonal balance as hormones direct nearly all sexual and reproductive functions. Disorders are often endocrine in origin. The organs of reproduction are particularly vulnerable to cancers that thrive on hormones, such as BREAST CANCER, OVARIAN CANCER, ENDOMETRIAL CANCER, PROSTATE CANCER, and TESTICULAR CANCER. Externally the reproductive system is vulnerable to injury and illness, to great extent through sexual activity. SEXUALLY TRANSMITTED DISEASES (STDS) can cause serious and sometimes life-threatening health conditions. STDs are a leading cause of INFERTILITY in women and can cause illness in newborns who are exposed during birth. Other factors that can affect reproductive health include exposures to chemicals such as pesticides or to radiation, which can damage the DNA of sperm or ova.

External factors are particularly important during pregnancy, when certain exposures at vulnerable points of fetal development can cause permanent injury. INFECTION with common viruses such as RUBELLA (German MEASLES) or measles can cause devastating BIRTH DEFECTS, as can taking certain drugs and medications. Nearly any substance the woman takes into her body may cross the PLACENTA to enter the fetus's BLOOD circulation. FETAL ALCOHOL SYNDROME, a constellation of physical birth defects and developmental abnormalities that occurs as a result of fetal exposure to ALCOHOL, is entirely preventable.

HEALTH CONDITIONS OF THE REPRODUCTIVE SYSTEM

ADENOMYOSIS	AMENORRHEA
BALANITIS	BARTHOLIN CYST
BENIGN PROSTATIC HYPERPLASIA (BPH)	BREAST CANCER
CERVICAL CANCER	CANCER OF THE PENIS
CHORDEE	CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)
CRYPTORCHIDISM	DYSMENORRHEA
ECLAMPSIA	ECTOPIC PREGNANCY
ENDOMETRIAL CANCER	ENDOMETRIAL HYPERPLASIA
ENDOMETRIOSIS	EPIDIDYMITIS
ERECTILE DYSFUNCTION	fibroadenoma
FIBROCYSTIC BREAST DISEASE	GYNECOMASTIA
HEMATOSPERMIA	HYDROCELE
HYPOGONADISM	INFERTILITY
INTRADUCTAL PAPILLOMA	KLINEFELTER'S SYNDROME
MASTALGIA	MASTITIS
NABOTHIAN CYST	NEONATAL JAUNDICE
ORCHITIS	OVARIAN CANCER
OVARIAN CYST	PAGET'S DISEASE OF THE BREAST
PARAPHIMOSIS	PEYRONIE'S DISEASE
PHIMOSIS	POLYCYSTIC OVARY SYNDROME (PCOS)
PREECLAMPSIA	PREMENSTRUAL SYNDROME (PMS)
PREMATURE OVARIAN FAILURE	PROSTATITIS
PRIAPISM	SEXUALLY TRANSMITTED DISEASES (STDS)
PROSTATE CANCER	TESTICULAR TORSION
SEXUAL DYSFUNCTION	UTERINE FIBROIDS
SPERMATOCELE	VAGINITIS
TESTICULAR CANCER	VULVODYNIA
TURNER'S SYNDROME	
UTERINE PROLAPSE	
VARICOCELE	

Traditions in Medical History

The high rate of maternal deaths from "childbirth FEVER" (puerperal fever) at the dawn of the era of antisepsis motivated Hungarian obstetrician Ignaz Philipp Semmelweis (1818–1861) to change his habits. In so doing, he transformed the practice of obstetrics and saved countless lives. By the middle of the 19th century scientists knew of the existence of microbes and their role in causing disease, though their mechanisms of infection remained a mystery. An emerging recognition was of the danger of infection for pathologists who performed autopsies. The slight wound from a slip of the scalpel was all too often fatal, causing systemic infection known as pathologist's pyemia. Semmelweis was the first to connect the two apparently

disparate conditions—puerperal fever and pathologist's pyemia—together.

Semmelweis practiced and taught at Vienna General Hospital, a major medical mecca of its time. Its maternity ward was very busy. As was the custom of the time, women attended by physicians went to one ward and women attended by midwives went to another ward. In 1847, the year of Semmelweis's epiphanic recognition, 20 to 35 percent of women who received care from doctors during childbirth died within weeks from puerperal fever. Only 2 percent of women who received their childbirth care from midwives met with similar fate.

Another customary practice of the time was for doctors to immediately autopsy patients who died, partly to provide education for student doctors. After his close friend died of a massive infection resulting from a wound suffered while conducting an autopsy, Semmelweis began to observe the patterns of illness in the maternity ward. He soon concluded that the practice of doctors freely moving between performing autopsies and attending to deliveries was the likely cause.

Semmelweis began to cleanse his hands with chlorinated lime before entering the childbirth ward and required his students to do the same. Though the caustic solution left the doctors' hands somewhat raw, nearly immediately the infection rate on their maternity ward dropped to 3 percent—much the same as the rate of infection on the midwifery ward. Midwives, of course, did not participate in autopsies. The change was a turning point in medicine's approach to childbirth. Within a decade antisepsis converged with the discovery of ANESTHESIA to vastly improve the safety and comfort of childbirth. When England's Queen Victoria received chloroform anesthesia during childbirth in 1853, she established a standard of acceptability for both improvements.

CESAREAN SECTION (surgical childbirth) also became a reasonable option for difficult deliveries, allowing doctors to save both mother and baby. Though ancient Chinese medical texts allude to a surgical childbirth procedure, cesarean section was an action of desperation to save the infant, generally carried out only when it was clear the mother had no chance of survival or had already died. Though popular mythology attributes the procedure and its name to the surgical birth of Rome's Julius Caesar, most medical historians believe such a correlation is highly unlikely. More likely is the derivation of the name from the Latin word *caesones*, the term applied to the infants who survived surgical extraction from their dying or dead mothers. Historical records document that Julius Caesar's mother lived long after her son's birth.

Breakthrough Research and Treatment Advances

The final decades of the 20th century brought pivotal advances in reproductive medicine. The first in vitro fertilization (IVF) baby—"test tube baby"—was born in England in 1978. Since then ASSISTED REPRODUCTIVE TECHNOLOGY (ART) has brought thousands of babies into the world. Today IVF is the cornerstone of treatment for infertility. Nearly 45,000 ART babies are born in the United States each year.

The coupling of advances in diagnostic imaging procedures and surgical techniques gave birth to the new subspecialty of fetal surgery, in which surgeons can operate on the unborn fetus to correct potentially devastating or fatal birth defects such as severe SPINA BIFIDA and congenital diaphragmatic HERNIA (incomplete formation or absence of the DIAPHRAGM). Technologic advances have also vastly improved the survivability of premature (preterm) infants, with some measures targeting efforts to maintain the pregnancy as long as possible and others focused on supporting the still-developing baby after birth.

Among the flurry of advances in pharmaceuticals at the turn of the 21st century, none attracted quite so much attention or sales as the phosphodiesterase (PDE) inhibitor medication to treat ERECTILE DYSFUNCTION, sildenafil. The trade name product Viagra catapulted to record sales, becoming the highest selling DRUG of all time within six months of its release. Sildenafil was the first convenient treatment for physiologically based erectile dysfunction, which affects about 25 million men in the United States.

The start of the 21st century also marked the end of a more than 50-year tradition in medical history when extensive research studies concluded that routine hormone replacement therapy (HRT) to treat menopause did not provide the health benefits widely attributed to it but instead signifi-

cantly raised a woman's risk for certain cancers. As well, there was no evidence that HRT reduced a woman's risk for CARDIOVASCULAR DISEASE (CVD), though supplemental estrogen did improve BONE health and reduce OSTEOPOROSIS. However, new drugs are able to accomplish the same effect without the increased risk for cancer that comes with estrogen supplementation.

A

abortion The end of a PREGNANCY before the FETUS is viable (capable of independent life). Abortion may occur spontaneously (commonly called miscarriage) or be induced to end a pregnancy. In the United States, federal law mandates the availability of induced abortion, and state laws regulate the definition of viability as it applies to induced abortion. The range of legal viability is 20 weeks to 24 weeks of gestational age. The clinical border for viability is generally 20 weeks or a fetal weight of 500 grams (about 1 pound). It is uncommon for a fetus delivered between 24 and 20 weeks and unlikely for a fetus born before 20 weeks of gestational age to survive. A full-term pregnancy is 42 weeks.

Spontaneous Abortion

Numerous factors may initiate spontaneous abortion. The most vulnerable period of pregnancy for spontaneous abortion is between 7 and 12 weeks. Doctors believe that most abortions that occur within this early stage of pregnancy occur because the conceived EMBRYO has congenital or chromosomal defects that are not survivable. About 15 percent of known pregnancies end in spontaneous abortion before the 12th week of pregnancy. Regardless of the cause and the stage of pregnancy, spontaneous abortion is often a traumatic loss for the woman and her partner.

Induced Abortion

An induced abortion is a procedure a woman chooses to undergo to end a pregnancy and may be therapeutic (medically necessary for the woman's health or because the fetus has known, nonsurvivable defects such as anencephaly) or elective termination of pregnancy. An induced abortion may be a surgical procedure called dilation and evacuation (D&E), performed under ANESTHESIA in a hospital operating room or in an AMBULATORY SURGICAL FACILITY, in which the doctor dilates the CERVIX and withdraws the contents of the UTERUS via suction (also called vacuum aspiration abortion). Before seven weeks an induced abortion may be a medical procedure, brought about by taking medications such as mifepristone (RU486), methotrexate, or misoprostol. These drugs, called abortifacients, prevent cell division (methotrexate, a CHEMOTHERAPY DRUG used to treat cancer) or implantation, or initiate uterine contractions (mifepristone and misoprostol).

Complications of Abortion

Uncontrolled bleeding (hemorrhage) and INFECTION are risks with either spontaneous or induced abortion. The abortion may be incomplete (some of the contents of CONCEPTION remain in the uterus), causing persistent or occasionally heavy bleeding. Persistent or heavy bleeding often requires DILATION AND CURETTAGE (D&C), a surgical procedure in which the doctor dilates the cervix and uses a curette to gently scrape the interior walls of the uterus. Undiagnosed GONORRHEA and CHLAMYDIA are the most common causes of postabortion infection. Infection requires treatment with ANTIBIOTIC MEDICATIONS. Either bleeding or infection may be life threatening; both require immediate medical evaluation and appropriate treatment. Rarely, abortion results in complications that can affect future FERTILITY.

Abortion, whether spontaneous or induced, is often an emotional experience for the woman and her partner. Guilt, sadness, and anger are common feelings that may persist for some time or reemerge years later. Induced abortion often has additional religious or philosophical implications.

See also BIRTH DEFECTS; CHILDBIRTH; CHROMOSOMAL DISORDERS; CONTRACEPTION; ECTOPIC PREGNANCY; FAMILY PLANNING; GENETIC DISORDERS; NEURAL TUBE DEFECTS; STILLBIRTH.

adenomyosis A condition in which the cells that make up the endometrium (the lining of the UTERUS) grow into the wall of the uterus (myometrium), forming benign (noncancerous) tumors that appear as thickenings or masses contained within the uterine wall. Adenomyosis nearly always occurs in women who have carried pregnancies to full term, causing doctors to believe the condition results from injury to the wall of the uterus as it stretches to accommodate the growth of the FETUS in the final weeks of PREGNANCY.

Adenomyosis may not cause symptoms; the doctor may discover its presence during evaluation for other health conditions affecting the uterus, such as DYSFUNCTIONAL UTERINE BLEEDING (DUB) or ENDOMETRIOSIS. The uterus may be tender to palpation (examination by touching) during PELVIC EXAMINATION. When symptoms do occur they may include PAIN during SEXUAL INTERCOURSE, unusually heavy menstrual bleeding, and intense menstrual cramping.

The diagnostic path may include ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI), though definitive diagnosis requires myometrial biopsy (laboratory examination of a tissue sample from the uterine wall). The gynecologist may use HYSTEROSCOPY to obtain the biopsy, or may examine tissue obtained through procedures to treat DUB such as DILATION AND CURETTAGE (D&C).

The monthly surge of hormones that cause the endometrium to thicken is responsible for symptoms; the engorged endometrial tissue causes pressure where it has infiltrated the myometrium. Because this hormonal cycle ends with MENOPAUSE (cessation of the menstrual cycle), adenomyosis then goes away. Treatment thus attempts to relieve symptoms until menopause occurs and may include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) or oral contraceptives (birth control pills) to regulate the hormonal balance that controls the MENSTRUAL CYCLE. When symptoms are severe and the woman does not desire further pregnancies, HYSTERECTOMY (surgery to remove the uterus) may be a treatment option. Because the infiltration into the myometrium is diffuse (spread out), it is not possible to surgically remove only the sites of adenomyosis. Adenomyosis does not affect FERTILITY or the capability of the uterus to again expand in pregnancy.

See also CONTRACEPTION; DYSMENORRHEA; ENDOMETRIAL CANCER; ENDOMETRIOSIS; UTERINE FIBROIDS.

adoption Accepting or relinquishing legal, social, and family responsibilities for a nonbiologic child. Adoption is an option within FAMILY PLANNING for people who desire children. Placing a child for adoption also an option in a circumstance of an unplanned PREGNANCY. About 150,000 adoptions take place in the United States each year. Adoptions may be open, in which there is direct or indirect contact between the biologic parents and the adoptive parents, or closed, in which the court seals the adoption records and biologic and adoptive parents do not know each other or anything about each other.

Each state in the United States has its own laws and procedures that regulate both sides of the adoption process. However, all states recognize and honor legal adoptions made in other states. Adoption laws regulate factors such as what information may be (or in some states, must be) made available to adult adopted children, the legal rights of biologic and adoptive parents, and the rights of biologic fathers who do not know their children were relinquished for adoption.

Countries around the world have their own laws and procedures for adoption that may or may not be consistent with practices in the United States. Though the United States generally recognizes foreign adoptions, federal immigration laws require specific evidence of legal adoption and other documentation. The US Department of State handles such matters. No matter the state or country, the legal issues of adoption are complex. It is prudent to obtain advice from a qualified adoption attorney before proceeding.

Health Concerns in Adopting a Child

Many adopted children come to their adoptive families with health concerns. Though it is ideal to have a full health history, including family history, for the adopted child, this does not often happen.

As a matter of course many adoptive families have the child undergo a comprehensive medical examination. Children adopted from other countries often have parasitic infections and other health conditions uncommon in the United States. FETAL ALCOHOL SYNDROME, congenital INFECTION with SEXUALLY TRANSMITTED DISEASES (STDS), HEPATITIS, RICKETS, TUBERCULOSIS, and hearing loss and VISION IMPAIRMENT are also common, especially with international adoptions. Though these are often treatable conditions, they do require prompt medical attention. Children older than one year may have emotional and psychologic problems as well. Sometimes, even in a closed adoption, the intermediary (adoption agency or attorney) is able to obtain more specific health information about the child to pass onto the adoptive parents. Conditions that require ongoing care, such as fetal ALCOHOL syndrome or developmental disabilities, are special needs.

Placing a Child for Adoption

Women have varying and often deeply personal reasons for placing their biologic children for adoption. Common reasons for being unable to retain parental rights include

- serious DRUG or alcohol abuse problems
- extreme youth or immaturity
- pregnancy that was the result of rape or incest
- health or disability issues that prohibit properly caring for a child

As well, mothers sometimes abandon their children without known reason. A woman who desires to place her child for adoption can notify her doctor, a community service agency, an adoption service, or an attorney. Typically there are no expenses to the relinquishing parent. Depending on circumstances the biologic mother may choose the adoptive family, especially if she is pregnant at the time she makes the decision to place the child for adoption.

The decision to place a child for adoption, which on the surface may appear straightforward, has lifelong emotional consequences for mother and child. The mother may feel guilty for "giving up" her child. The child, when old enough to understand what adoption means, may feel abandoned regardless of the circumstances of the adoptive family. It is important for adoptive families to be loving yet as open as possible about questions adoptive children may ask. Many communities have SUPPORT GROUPS for adoptive parents, adopted children, and people who placed their children for adoption. Support groups can help people share their concerns, feelings, and solutions to common problems.

Parenting and family are life experiences that have challenges and accomplishments, perils and joys, no matter what their configurations. For many adults who adopt, adoption brings to fruition a lifelong dream to raise and parent a child, either starting or adding to a family. And for many children who are adopted, adoption is daily evidence that someone wants them and loves them very much.

See also CULTURAL AND ETHNIC HEALTH CARE PERSPECTIVES; GESTATIONAL SURROGACY; PARENTING.

aging, reproductive and sexual changes that occur with The reproductive system, male or female, is intact but immature at birth and remains immature until the onset of PUBERTY around age 12. Researchers do not know what triggers the physiologic events that take place to initiate reproductive and sexual maturity. However, these events result in the development of SECONDARY SEXUAL CHARACTERISTICS, sex drive and interest, and the ability to produce new life. Male FERTILITY extends from puberty to the end of life, though may diminish somewhat in late old age. Female fertility is finite, starting at MENARCHE (the onset of the MENSTRUAL CYCLE) and ending with MENOPAUSE (the conclusion of the menstrual cycle). Only for a few days each month is a woman capable of CONCEPTION.

The hormones of sexual and reproductive maturity have numerous and far-reaching effects in the body. Men and women alike have the spectrum of sex hormones: ESTROGENS and ANDROGENS. Androgens dominate in men; estrogens dominate in women. These hormones account for secondary sexual characteristics and reproductive ability as well as MUSCLE mass and STRENGTH, BONE DENSITY, lipid metabolism, aspects of cardiovascular function, cognitive clarity, BRAIN function, mood, and emotion.

Age-related hormonal changes are most prominent in women, who experience significant transformation in their bodies with menopause. The cessation of OVULATION means a pronounced drop in estrogen within the body, affecting not only reproductive capability but also the functions of nearly every system in the body. Health concerns that arise from these changes include increased risk for OSTEOPOROSIS, CARDIOVASCULAR DISEASE (CVD), and certain types of cancer. Men also experience age-related changes in sexuality and reproductive function. A man's testosterone level peaks when he is in his early 20s and gradually declines with each decade of life. By age 60 most men have about half the testosterone they had at age 25. This decline results in changes such as diminished muscle mass and strength and male pattern baldness (ALOPECIA). A man's risk for PROSTATE CANCER significantly increases after age 60. Though a man can still father children even into his 80s, declining testosterone affects LIBIDO (sex drive) and erectile function.

See also ANDROPAUSE; BENIGN PROSTATIC HYPERPLASIA (BPH); ERECTILE DYSFUNCTION; LIFESTYLE AND HEALTH; MENSTRUATION; PROGESTERONE.

alpha fetoprotein (AFP) A protein the LIVER produces. In PREGNANCY the amount of AFP in the woman's BLOOD circulation increases, reflecting the activity of the FETUS's liver as it develops and becomes functional. A blood test measures AFP in the woman's blood circulation early in the second trimester, between 15 and 22 weeks of pregnancy.

Elevated AFP levels in pregnancy may indicate a multiple pregnancy, NEURAL TUBE DEFECTS or defects in the structure of the abdominal wall that allow the organs of the gastrointestinal system to form outside the body. Chronic liver disease, such as HEPATITIS or CIRRHOSIS, also elevates AFP. Excessive ALCOHOL consumption and cigarette smoking are common causes of falsely high measures. Low AFP levels may indicate a pregnancy that is not as advanced as the woman believes or suggest the chromosomal disorder DOWN SYNDROME.

Other health circumstances elevate AFP blood levels in nonpregnant women and in men. Among them are liver disease, including LIVER CANCER, TESTICULAR CANCER in men, and OVARIAN CANCER in women. Deviations from normal AFP levels in pregnancy suggest circumstances that may warrant further medical evaluation such as ULTRASOUND, AMNIOCENTESIS, and CHORIONIC VILLI SAMPLING (CVS).

See also ALCOHOLISM; CHROMOSOMAL DISORDERS; GENETIC DISORDERS; PRENATAL CARE.

amenorrhea The absence of menstrual periods. Primary amenorrhea occurs when a young woman does not begin menstruating by age 16; secondary amenorrhea occurs in women who have been menstruating and then stop (miss six or more consecutive periods).

Primary amenorrhea may result from GENETIC DISORDERS such as TURNER'S SYNDROME or from hormonal disorders such as pituitary ADENOMA (a tumor of the PITUITARY GLAND) or HYPOTHYROIDISM (underactive THYROID GLAND). PREGNANCY is the most common cause of secondary amenorrhea. Other factors that may cause either primary or secondary amenorrhea include intense physical exercise, excessive body weight (OBESITY), and extreme underweight such as may result from EATING DISORDERS.

Amenorrhea is a symptom of underlying conditions that affect the function of the OVARIES rather than itself a health condition. Because the hormones the ovaries produce affect many other functions within the body, it is important to identify its cause. Unresolved primary amenorrhea may have consequences such as permanent INFERTILITY and failure to develop SECONDARY SEXUAL CHARACTERISTICS.

See also BODY MASS INDEX (BMI); DYSMENORRHEA; EXERCISE AND HEALTH; FERTILITY; HORMONE; OBESITY AND HEALTH; OVULATION; PRIMARY OVARIAN FAILURE; WEIGHT LOSS AND WEIGHT MANAGEMENT.

amniocentesis A diagnostic procedure to withdraw a sample of AMNIOTIC FLUID from the UTERUS of a pregnant woman to obtain information about the health status of the FETUS. Obstetricians use amniocentesis, typically performed during the second trimester of PREGNANCY, to help diagnose GENETIC DISORDERS and health conditions of the developing fetus such as DOWN SYNDROME or SPINA BIFIDA and other NEURAL TUBE DEFECTS. Amniotic fluid contains cells from the fetus that can provide a KARYOTYPE (representation of CHROMOSOME pair-

ings) and other genetic information about the fetus. The amniotic fluid may also provide information about the woman's health, such as whether any INFECTION is present, and help doctors determine whether the fetus's lungs are mature.

To perform amniocentesis, the obstetrician first numbs a small area on the surface of the woman's abdomen, either with a topical anesthetic spray or an injection of local anesthetic. The obstetrician then inserts a long needle through the woman's abdominal wall into the amniotic sac and withdraws about 20 milliliters (less than an ounce) of amniotic fluid for laboratory analysis. ULTRASOUND helps determine the position of the fetus and the ideal insertion and placement of the needle so as to avoid injury to the fetus. Because the laboratory must first cultivate cells from the amniotic fluid, GENETIC TESTING results take two to three weeks.

Risks of amniocentesis include bleeding, infection, injury to the fetus, and spontaneous ABORTION (loss of the pregnancy). Some women feel temporary discomfort during the procedure, and many women find the requisite full BLADDER (necessary for the ultrasound) causes pressure and other discomforts. Some women experience mild cramping and slight bleeding for a day or two after the amniocentesis.

See also ALPHA FETOPROTEIN (AFP); ANESTHESIA; CHORIONIC VILLI SAMPLING (CVS); CHROMOSOMAL DISORDERS; CONGENITAL ANOMALY; PRENATAL CARE.

amniotic fluid The liquid that surrounds the developing FETUS within the amniotic sac, a membranous structure that forms inside the UTERUS in PREGNANCY. The amnion, the inner membrane of the amniotic sac, begins producing amniotic fluid at about two weeks of gestation. The amniotic fluid, which is mostly water, cushions the fetus against changes in temperature as well as jarring and bumps from outside the womb. The composition of amniotic fluid changes somewhat over the duration of pregnancy though typically includes, in addition to water, electrolytes, lipids, proteins, metabolic byproducts, and cells that the fetus sheds. These cells provide the DNA that AMNIOCENTESIS uses to assess the health of the fetus.

Amniotic fluid is essential not only to protect the fetus but also for proper fetal development. In the second trimester the fetus swallows and "breathes" to take amniotic fluid into its STOMACH and LUNGS, which is necessary for development of the structures and functions of the pulmonary and gastrointestinal systems. The fetus also begins contributing URINE to the composition of the amniotic fluid. By the third trimester the amniotic fluid replenishes itself about every three hours and reaches a volume of approximately 500 milliliters. The amniotic sac ruptures when CHILDBIRTH is imminent, sending a flood of amniotic fluid from the woman's VAGINA. This process is the "breaking water" that often heralds the onset of pregnancy's final stages, labor and delivery.

A lower than normal volume of amniotic fluid is oligohydramnios, which may constrict the movement of the fetus to an extent that causes abnormal musculoskeletal development, intrauterine growth retardation, and other problems. A greater than normal volume of amniotic fluid is polyhydramnios, which may indicate NEURAL TUBE DEFECTS or BIRTH DEFECTS of the KIDNEYS or gastrointestinal structures. Polyhydramnios is sometimes present when the mother has diabetes. It presents increased risk for UMBILICAL CORD problems such as umbilical cord prolapse (the umbilical cord enters the vagina before the fetus's head as birth begins, a potentially life-threatening scenario for the fetus), as well as large for gestational age or macrosomia (birth weight significantly higher than normal).

For further discussion of amniotic fluid within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also CESAREAN SECTION.

andropause A term sometimes used to describe the physical and emotional changes men experience at midlife. The amount of TESTOSTERONE, the primary male sex HORMONE, in a man's BLOOD circulation begins to slowly and steadily decline after reaching its peak in the early to middle 20s. By age 75, testosterone levels are typically about half of what they were at age 25. Though this is still an adequate level of testosterone to maintain masculinity, the decline accounts for some of the physical changes characteristic of midlife in men: conversion of MUSCLE to fat, redistribution of body

fat, and sometimes diminished energy and LIBIDO (sex drive). Some men experience clinical DEPRESSION, loss of BONE mass, ERECTILE DYSFUNCTION, and other symptoms as a consequence of lower testosterone levels. Some researchers believe the decline in testosterone levels contributes to the increased risk for HEART ATTACK as a man gets older.

Doctors may recommend prescription hormone supplementation with ANDROGENS (testosterone or testosterone precursors) for men who have unacceptable symptoms. However, the long-term therapeutic value and possible risks of such treatment remain uncertain. Some men take the over-the-counter product DEHYDROEPIANDROSTERONE (DHEA), available in the United States as a dietary supplement, as an androgen precursor (a substance the body converts to testosterone during its METABOLISM). There are few clinical studies to provide clear evidence of whether this is effective or safe. Some doctors believe as long as the DHEA does not push testosterone levels beyond the normal range, the risk for adverse health effects is minimal. However, other doctors worry that sustained increases in blood testosterone levels in men over age 50 may increase the risk for PROSTATE CANCER and CARDIOVASCULAR DISEASE (CVD).

See also ADRENAL INSUFFICIENCY; AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; ANABOLIC STEROIDS AND STEROID PRECURSORS; HORMONE-DRIVEN CANCERS; MENOPAUSE.

Apgar score A standardized measure of an infant's health status, typically assessed one minute and five minutes after birth. Anesthesiologist Virginia Apgar (1909–1974) developed the scoring system that bears her name in 1953, assigning a point value of 0, 1, or 2 to each of five categories of vital function (BREATHING, HEART RATE, REFLEX response, MUSCLE tone, and SKIN color) and reporting their sum as the overall Apgar score. Today the Apgar score is an international standard to assess whether a newborn needs resuscitation (lifesaving measures) and to evaluate the success of resuscitative efforts. The highest score possible is 10; doctors consider a score between 7 and 10 to reflect good health in the infant. A score between 4 and 7 bears monitoring and perhaps supportive care such as suctioning of the airways or supplemental oxygen. A score of 3 or lower indicates a life-threatening or critical circumstance for the infant.

See also CHILDBIRTH; PREMATURE BIRTH.

assisted reproductive technology (ART) Medical interventions to produce PREGNANCY. The US Centers for Disease Control and Prevention (CDC), which has a mandate under federal law to report the success rates of ART at FERTILITY clinics in the United States each year, defines ART as any method that involves manipulation of both SPERM and OVA (eggs). Other methods to aid fertility may use interventions such as HORMONE therapies to stimulate OVULATION (the release of ova) in the woman or techniques such as intrauterine artificial insemination (placement of sperm within the UTERUS) to improve sperm viability. ART typically

APGAR SCORES

Apgar Score	0	1	2
BREATHING	not breathing	slow or irregular breathing	20 to 50 breaths per minute, regular rhythm
HEART RATE	no heart rate	< 100 beats per minute	100 to 104 beats per minute
REFLEX response	no response to nasal stimulation	facial grimace with nasal stimulation	sneeze or cough with nasal stimulation
MUSCLE tone	flaccid	some flexing of the arms and legs	active movement
SKIN color	cyanotic (bluish gray)	cyanotic limbs	pink

becomes an option to treat INFERTILITY when less invasive approaches fail to result in pregnancy or when health factors compromise fertility in both partners.

Methods of ART

Most methods of ART involve uniting sperm and ova outside the body and returning the results to the woman's body. There are four commonly used methods of ART:

- In vitro fertilization (IVF) is the most common method of ART. The technologist mixes sperm and several ova together in a laboratory container. The sperm penetrate and fertilize the ova. After the zygotes form, the fertility specialist transfers two to four zygotes into the woman's uterus. IVF eliminates issues of sperm motility, sperm antibodies, and blocked FALLOPIAN TUBES. It may be an appropriate choice for male factor infertility, female factor infertility, or combined factor infertility and may use donor eggs, donor sperm, or eggs and sperm collected from the woman and her partner.
- GAMETE intrafallopian transfer (GIFT) mixes ova and sperm in a thin catheter and transfers the mixture directly to the woman's fallopian tube. Fertilization takes place within the fallopian tube and the ZYGOTE travels to the uterus to implant. GIFT may be the ART method of choice when the woman has healthy fallopian tubes and male factor infertility is the primary issue. GIFT is also an acceptable method of assisted CONCEPTION within cultures and belief systems in which fertilization must take place inside the woman's body.
- Intracytoplasmic sperm injection (ICSI) is somewhat like IVF though leaves less to chance. The technologist extracts a single sperm from the collected sperm and injects it into an ovum to fertilize the ovum. The fertility specialist then transfers the zygote into the woman's fallopian tube or uterus. ICSI is often the ART method of choice for male factor infertility, especially when the man's sperm count is very low.
- Zygote intrafallopian transfer (ZIFT) begins with IVF though the fertility specialist then uses laparoscopy to place two to four zygotes into the woman's fallopian tube. ZIFT is a common ART choice for male factor infertility and may be appropriate when IVF has not succeeded. Fertility specialists believe the embryos that result from IVF may be more fragile than those that develop within the fallopian tube.

Before any of these methods can occur, the fertility clinic must obtain ova and sperm, either from the woman and man undergoing ART or from donors. Ova retrieval begins with injection of a hormone, human chorionic gonadotropin (hCG). Then, 36 hours later, the fertility specialist aspirates (gently suctions away) the ripened ova using a catheter inserted into the pelvic cavity through the vagina with ULTRASOUND to visualize and guide the process. Sperm retrieval may occur through EJACULATION or the fertility specialist may extract sperm, using needle and syringe, directly from the man's testicle (EPIDIDYMIS). Sperm extraction does not require hormones.

Success of ART

About 45,000 births occur in the United States each year as a result of ART, representing about a 25 percent success rate overall for ART. However, many couples undergo multiple ART attempts, and the rate of pregnancy correlates to the woman's age with a precipitous drop after age 35. Nearly a third of ART conceptions are multiples (twins or higher), a consequence of the practice of implanting multiple embryos to improve the likelihood of a viable pregnancy (pregnancy that carries to full term with delivery of a healthy baby). Some ART methods are more successful than others, depending on the infertility circumstances. As well, the ART may succeed in generating a pregnancy but the pregnancy does not carry to term. The CDC reports annual ART success rates for pregnancies and live births according to ART method and by fertility center. The report is available at the CDC's Web site (www.cdc.gov/art).

Concerns and Risks of ART

Despite significant advances in understanding and technology, much about fertility remains a mystery. The long-term risk associated with hormone use to stimulate ovulation for egg retrieval in

women is probably negligible but remains unknown. Risks for chromosomal and genetic damage also remain unknown. However, since the first successful IVF in 1978, hundreds of thousands of babies born through ART methods have reached adulthood and many now have children of their own with both parent and child healthy. It is important for people considering ART to know as much as possible about their family health histories and to fully understand the possible complications and risks for the methods of ART they are considering, because knowledge in this area changes rapidly.

See also ADOPTION; FAMILY PLANNING.

B

balanitis INFLAMMATION of the glans, the tip of the PENIS, usually the consequence of a bacterial or fungal (yeast) INFECTION. Balanitis is more likely to occur in uncircumcised men, as the foreskin can provide the moist, warm environment that supports the growth of pathogens. Diligent PERSONAL HYGIENE is especially important in uncircumcised men to keep the area beneath the foreskin clean and dry to prevent irritation and infection. The diagnostic path may include laboratory culture of a sample swabbed from the inflamed area to determine the cause of the infection, with appropriate ANTIBIOTIC MEDICATIONS or ANTIFUNGAL MEDICATIONS to treat the infection. Medications may be oral (taken by MOUTH), topical (applied to the penis), or both.

Most balanitis clears with treatment and hygienic measures. A potentially serious complication is PHIMOSIS, in which the foreskin forms adhesions to the glans and becomes unretractable. Phimosis further complicates balanitis and may require CIRCUMCISION (surgical removal of the foreskin).

See also BACTERIA; CANDIDIASIS; CHLAMYDIA; FUNGUS; HUMAN PAPILLOMAVIRUS (HPV); PATHOGEN; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

Bartholin's cyst A fluid-filled enlargement of a Bartholin's gland. There are two Bartholin's glands, one on each side of the entrance to the VAGINA. Normally undetectable, the Bartholin's glands produce secretions that lubricate the vaginal opening. A cyst may form when the duct that allows the secretions to drain from the gland becomes blocked (occluded). The secretions continue to accumulate but have no exit, causing the gland to gradually enlarge. The enlargement may become quite large before a woman can detect it, and often causes no symptoms until its size causes discomfort.

The gynecologist can diagnose a Bartholin's cyst on the basis of its appearance. Treatment is to drain the cyst, after which the gland returns to normal function. The gynecologist may place a tiny tube temporarily into the cyst to allow the accumulated fluid to drain, or may make a small incision to release the fluid, then suture the incision open to maintain drainage. These procedures are usually performed in the gynecologist's office with local ANESTHESIA to first numb the area. Occasionally an INFECTION develops within a Bartholin's cyst, which requires a course of treatment with ANTIBIOTIC MEDICATIONS.

See also VAGINITIS.

benign prostatic hyperplasia (BPH) A noncancerous enlargement, also called benign prostatic hypertrophy, of a man's PROSTATE GLAND. BPH is common in men over age 60 and is a condition of aging. Though BPH is not cancer, some men who have BPH do develop PROSTATE CANCER. Researchers do not know what causes BPH though believe the changes in HORMONE levels and ratios that naturally occur with aging probably are key.

BPH develops when the number of cells in the prostate gland increases, causing the gland to grow. The prostate gland encircles the URETHRA like a cuff at the neck of the BLADDER. BPH typically constricts the urethra, either by compressing it from the outside or blocking it from the inside if prostate cells invade the urethral walls. The resulting occlusion interferes with URINATION.

Symptoms and Diagnostic Path

The symptoms of BPH develop gradually over time and may include

- hesitation when urinating (stopping and starting during the flow)
- URINARY URGENCY and URINARY FREQUENCY, especially at night (NOCTURIA)
- dribbling URINE after the man finishes urinating
- HEMATURIA (bloody urine)
- URINARY INCONTINENCE

The diagnostic path includes a BLOOD test to measure the PROSTATE-SPECIFIC ANTIGEN (PSA) level and a DIGITAL RECTAL EXAMINATION (DRE), which allows the doctor to palpate (feel) the prostate gland through the wall of the RECTUM. This examination helps determine whether the enlargement of the prostate gland is likely benign (the gland feels soft to palpation) or suspicious (the gland feels hard or irregular). Further diagnostic procedures may include measurement of postvoiding urine (urine that remains in the bladder after urination), ULTRASOUND of the bladder, and occasionally CYSTOURETHROGRAM to rule out other causes of the symptoms.

Treatment Options and Outlook

Treatment depends on the nature of the prostate gland's overgrowth, the severity of symptoms, and the man's preferences. Treatment options include

- MINIMALLY INVASIVE SURGERY to remove excess prostate gland tissue
- transurethral resection of the prostate (TURP), an OPERATION in which the urologist removes portions of the prostate gland using an endoscopic instrument inserted through the urethra
- PROSTATECTOMY, an operation to entirely remove the prostate gland
- alpha blocker medications, which relax smooth MUSCLE tissue to improve the flow of urine
- 5-alpha reductase inhibitor medications such as finasteride and dutasteride, which block the conversion of TESTOSTERONE to dihydrotestosterone (DHT) to slow the growth of prostate gland cells
- herbal remedies such as SAW PALMETTO, stinging nettle extract, SOY protein and soybean products, and flaxseed oil

MEDICATIONS TO TREAT BENIGN PROSTATIC HYPERPLASIA (BPH)

alfuzosin	doxazosin
dutasteride	finasteride
prazosin	tamsulosin
terazosin	

Prostatectomy is the only cure for BPH, though it has significant risks and potential complications. Most men are able to achieve long-term relief of symptoms through medication or minimally invasive procedures.

Risk Factors and Preventive Measures

Age is the primary risk factor for BPH. BPH is rare in men under age 50 and nearly always present in men over age 70. There are no known methods for preventing BPH. It is important for men over age 50 to undergo recommended preventive screening and examination for prostate cancer, as the risk for prostate cancer also increases with age and its early symptoms are indistinguishable from those of BPH.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; BLADDER CANCER; ENDOSCOPY; HORMONE-DRIVEN CANCERS; SURGERY BENEFIT AND RISK ASSESSMENT; URETHRAL STRICTURE.

birth control See CONTRACEPTION.

breast The mammary gland. Both men and women have breasts. Each person's two breasts are close to but not exactly the same size and shape. Breasts vary widely in appearance among both men and women.

At PUBERTY the female sex hormones (primarily ESTROGENS) in girls cause the glandular components of the breast to enlarge, establishing the potential to produce milk. The nipple also enlarges as does the glandular tissue surrounding it, the areola. Enlarged breasts are among the female SECONDARY SEXUAL CHARACTERISTICS. Female breasts fill out with adipose (fatty) tissue and connective tissue in addition to its glandular structures, becoming rounded, and extend out from the chest. The male sex hormones (primarily TESTOSTERONE) have the opposite effect in boys, causing the glandular components to all but disappear. In adulthood the male breasts remain relatively flat against the chest.

The glandular components of the adult female breast are the lactiferous glands, which can produce and secrete milk, and the lactiferous ducts, which store milk. Fatty tissue accumulates around these structures, called lobules. Supportive connective fibers called Cooper ligaments group the lobules into lobes. Each breast contains between 15 and 20 lobes. Milk production, called lactation, occurs under the stimulation of PROLACTIN, a HORMONE the PITUITARY GLAND begins to secrete after CHILDBIRTH. Lactation may continue for as long as the woman continues BREASTFEEDING. Another hormone, OXYTOCIN, stimulates the release of milk from the breast. The breasts may become significantly larger (up to three times their prepregnancy size) while the woman is breastfeeding. When breastfeeding stops the lactiferous structures (glands and ducts) shrink and the breasts return to their normal size.

The breasts are also sources of sexual stimulation and arousal for women and for men, both by touch and visually. During sexual arousal and at ORGASM the nipples become firm and erect. A woman's breasts may become uncomfortably tender and sometimes swollen during the luteal phase of the MENSTRUAL CYCLE, in response to the elevation of estrogens in the BLOOD circulation.

At MENOPAUSE the glandular tissue in the breast shrinks and the breast structure becomes much less dense. At this time a woman's risk for BREAST CANCER increases significantly. Current preventive health guidelines recommend routine MAMMOGRAM (X-RAY of the breast) beginning at age 40 for most women, and beginning earlier and occurring more frequently in women who have high risk for developing breast cancer. Health experts recommend that all women, beginning at the conclusion of puberty, perform monthly BREAST SELF-EXAMINATION as a method of early detection for BREAST HEALTH concerns, including lumps that may be cancerous.

HEALTH CONDITIONS THAT CAN AFFECT THE BREASTS

BREAST CANCER	fibroadenoma
FIBROCYSTIC BREAST DISEASE	GYNECOMASTIA
INTRADUCTAL PAPILLOMA	MASTALGIA
MASTITIS	PAGET'S DISEASE OF THE BREAST

For further discussion of the breast within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also LIGAMENT; PREMENSTRUAL SYNDROME (PMS); TURNER'S SYNDROME.

breast cancer A malignant (cancerous) tumor that arises in the BREAST. There are many types of breast cancers, some of which are HORMONE driven (draw sustenance from ESTROGENS or PROGESTERONE) and others that are not. Primary breast cancer originates in the breast; secondary breast cancer metastasizes (spreads) to the breast from an origin elsewhere in the body. Breast cancer may also metastasize to other sites in the body such as the LUNGS or bones.

Breast cancer is the most common cancer among American women; doctors in the United States diagnose breast cancer in about 200,000 women each year. Breast cancer is currently second to LUNG CANCER as the leading cause of deaths due to cancer among women. However, significant advances in the early 2000s in understanding the mechanisms of breast cancer cells and the resulting development of new treatments are changing the landscape of breast cancer.

Genetic factors The genes BRCA-1/BRCA-2 were the first genes conclusively linked to cancer. Inherited mutations in these genes significantly increase a woman's risk for breast cancer and OVARIAN CANCER. Researchers continue to study these mutations for ways to take advantage of them for preventing or treating cancers in women who have either or both mutations.

Other mutations are not hereditary but instead occur over time, the consequence of molecular damage that becomes cumulative over time. Researchers have identified nearly two dozen genes that influence cell proliferation (cell growth and division) in some way. One of the most significant is the *her-2* GENE (human epidermal growth factor receptor 2, also called HER-2/neu) gene, located on CHROMOSOME 17. The *her-2* gene expresses (directs the production of) certain protein receptors on the surfaces of cell membranes. The receptors allow binding with the HER-2/neu protein, a protein that instructs the cell to grow and divide. Mutations in the *her-2* gene cause increased numbers of HER-2/neu receptors on cells, allowing greater HER-2/neu binding. This

process, called overexpression, alters the way in which the cells grow and divide.

Hormonal factors Breast cancer cells may have receptors on the surfaces of their cell membranes for estrogen, progesterone, or both. These are hormone-positive cancer cells—designated as estrogen positive (ER+) or progesterone positive (PR+), with an accompanying percentage or numeric value that identifies the relative proportion or number of positive hormone receptors.

Immune factors The risk for breast cancer, like most types of cancer, increases with age. As immune function diminishes with age, so does the body's ability to protect itself against health conditions such as cancer. Researchers are exploring the roles foods and NUTRIENTS play in supporting the IMMUNE SYSTEM's ability to identify, contain, and eliminate cancer cells that develop. Immune dysfunction appears to play a direct role in one rare but aggressive type of breast cancer, inflammatory breast cancer (IBC). In IBC the breast cancer cells collect in the LYMPH vessels, causing INFLAMMATION within the breast rather than forming a discreet tumor.

TYPES OF BREAST CANCER

ADENOCARCINOMA	infiltrating comedocarcinoma
infiltrating intraductal CARCINOMA (IDC)	infiltrating lobular carcinoma
intraductal carcinoma	inflammatory BREAST cancer (IBC)
lobular carcinoma in situ (LCIS)	mucinous (colloid) carcinoma
noninfiltrating intraductal carcinoma	noninfiltrating comedocarcinoma
papillary carcinoma	PAGET'S DISEASE OF THE BREAST
	tubular carcinoma

Breast cancer in men Though people think of breast cancer as a woman's condition, men also can develop breast cancer. Breast cancer in men is rare, occurring in 1 man for every 100 women who develop it. Men develop fewer types of breast cancers as well, because their breasts do not have the glandular tissue prevalent in the breasts of women. The types of breast cancers that occur in men are ADENOCARCINOMA, ductal carcinoma in situ (DCIS), and infiltrating ductal carcinoma (IDC). Men can also develop PAGET'S DISEASE OF THE BREAST, a condition in which cancer cells migrate into the SKIN around the nipple, though this uncommon type of cancer is even more rare in men than in women. Symptoms of male breast cancer are the same as symptoms breast cancer in women. Many treatment options are also the same. Doctors diagnose about 1,700 men with breast cancer each year in the United States.

Symptoms and Diagnostic Path

In most situations the only symptom of breast cancer is a lump that the woman, her health-care provider, or a mammogram detects. Most breast cancer tumors do not hurt. Other symptoms of breast cancer may include

- nipple discharge, typically watery or sometimes blood tinged
- dimpling of the skin on the surface of the breast
- changes in the appearance of, or inversion of, the nipple
- changes in the shape or profile of the breast
- general sense of tiredness or lack of energy

The diagnostic path may include diagnostic mammogram, breast ULTRASOUND, fine-needle aspiration biopsy of the lump to obtain cell samples for laboratory examination, or excisional biopsy to remove the lump and provide tissue for laboratory examination. Excisional biopsy provides conclusive diagnosis. The pathologist determines the hormonal sensitivity of the cancer cells (estrogen or progesterone receptor positive) and whether they are *her-2* positive or negative. Many cancer centers conduct further testing to analyze the genetic composition of the cancer cells. Such testing provides insights into how the cancer cells grow and often reveals their vulnerabilities, allowing precisely targeted treatments. As well, the pathologist evaluates the size and characteristics of the tumor to determine its grade (level of abnormality in the cells) and stage (extent of the tumor). These factors in combination are crucial for determining appropriate CANCER TREATMENT OPTIONS AND DECISIONS.

Treatment Options and Outlook

Primary treatment for early stage breast cancer of any type is surgery to remove the cancer, which may be lumpectomy (removal of the lump and a

safe margin of normal tissue), segmental MASTECTOMY (removal of the one quarter segment of the breast that contains the tumor), simple mastectomy (removal of the breast), or modified radical mastectomy (removal of the breast and some surrounding tissue along with SENTINEL LYMPH NODE DISSECTION).

Nearly all women who have surgery for breast cancer also receive adjuvant (follow-up) therapy, which may include RADIATION THERAPY, CHEMOTHERAPY, HORMONE THERAPY, or MONOCLONAL ANTIBODIES (MABS) therapy, either singularly or in combination. These therapies also may be primary treatment for later stage and recurrent breast cancers. In the late 1990s hormone therapy and MAbs therapy (also called biological response modifier therapy or IMMUNOTHERAPY) became the frontrunners in adjuvant therapy for HORMONE-DRIVEN CANCERS—tumors sensitive to estrogen (ER+) or progesterone (PR+)—and HER-2/neu-positive tumors, respectively. In late 2005 the National Comprehensive Cancer Network (NCCN) issued revised treatment guidelines for breast cancer in which the cancer's hormone and *her-2* status are the primary factors for deciding the type and course of adjuvant therapy, with the traditional practice of evaluating tumor size and the degree of METASTASIS being a secondary step.

Hormone therapy for breast cancer Hormone therapy targets suppression of estrogen and progesterone in the woman's body. Among the therapies to achieve this goal are

- selective estrogen receptor modulators (SERMs), drugs that bind with estrogen receptors to keep estrogen from doing so; SERMs have some estrogen-like qualities that help maintain BONE DENSITY and lipid METABOLISM
- estrogen receptor downregulators (ERDs), which first bind with estrogen receptors and then destroy them
- aromatase inhibitors, which block the action of aromatase, an enzyme that converts ANDROGENS naturally occurring in body tissues such as fat into estrogen

Hormone therapy for breast cancer is effective in women who are past MENOPAUSE or who have no ovarian function due to surgical removal of the OVARIES (OOPHORECTOMY) or chemical suppression of ovarian function (medications such as goserelin and leuprolide). Blocking estrogen production cuts off the supply of estrogen to cancer cells that require it, preventing the cells from growing. Side effects that may occur with hormone therapy include JOINT PAIN, NAUSEA, DIARRHEA, HEADACHE, and HOT FLASHES.

SERMs were the first effective hormone therapy drugs (tamoxifen came on the market in the 1980s). They generally have therapeutic value for about five years, after which their ability to bind with estrogen receptors diminishes. Oncologists may recommend taking a SERM for five years and then switching to an aromatase inhibitor, which does not appear to have time-limited usefulness. Aromatase inhibitors and ERDs are too new in clinical practice to know their long-term effectiveness.

HORMONE THERAPY DRUGS TO TREAT BREAST CANCER

Selective Estrogen Receptor Modulators (SERMs)

raloxifene (Evista)
tamoxifen (Nolvadex)
toremifene (Fareston)

Aromatase Inhibitors

anastrazole (Arimidex)
exemestane (Aromasin)
letrozole (Femara)

Estrogen Receptor Downregulators (ERDs)

fulvestrant (Faslodex)

Trastuzumab (Herceptin) Trastuzumab, a monoclonal antibody, specifically targets *her-2* receptors on breast cancer cells. First produced in the early 1970s, trastuzumab demonstrated its effectiveness against *her-2* positive breast cancer in the 1980s and became the cornerstone of treatment for *her-2* positive metastatic breast cancer in the 1990s. Because trastuzumab so narrowly targets breast cancer cells, it causes few side effects. However, one significant, though rare, SIDE EFFECT is HEART FAILURE. In the first decade of the 2000s, oncologists began administering trastuzumab for *her-2* positive stage 2, stage 3, and stage 4/metastatic breast cancers along with combination chemotherapy.

CHEMOTHERAPY AGENTS TO TREAT BREAST CANCER	
capecitabine	cyclophosphamide
docetaxel	doxorubicin
epirubicin	5-fluorouracil (5FU)
gemcitabine	paclitaxel
vinorelbine	

Risk Factors and Preventive Measures

Age is the primary risk factor for breast cancers of all types, with the likelihood of developing breast cancer reaching one in two for women 85 and older. Hereditary factors (such as BRCA-1/BRCA-2) influence about 5 percent of breast cancers. Lifestyle factors that contribute to nonhereditary breast cancers include EATING HABITS that feature high-fat foods, lack of physical exercise, cigarette smoking, and excessive ALCOHOL consumption.

There is a strong correlation between OBESITY and breast cancer, though researchers do not know whether this is a circumstance of excess body fat or the consequence of eating habits and physical inactivity. Fat cells convert androgens to estrogen, raising the level of estrogens in the blood circulation. Continued exposure to elevated levels of estrogen is a risk factor for breast cancer as well as other hormone-driven cancers.

It is not possible at present to completely prevent breast cancer. However, lifestyle improvements can significantly reduce the risk of developing breast cancer. Regular breast examination from a health care provider, breast self-examination, and mammograms make possible early detection of breast cancer, which establishes the most ideal circumstances for successful treatment.

See also CANCER PREVENTION; DIET AND HEALTH; FIBROCYSTIC BREAST DISEASE; INTRADUCTAL PAPILLOMA; MOLECULARLY TARGETED THERAPIES; MUTATION; OBESITY AND HEALTH; ONCOGENES; SMOKING AND HEALTH; STAGING AND GRADING OF CANCER; SURGERY BENEFIT AND RISK ASSESSMENT.

breastfeeding The process of nourishing an infant with milk the mother's breasts produce. Health experts recommend breastfeeding at least for the first six months of life when possible. BREAST milk provides the ideal nutritional balance for the infant. It also conveys important antibodies to the infant, helping provide immune protection while the infant's own IMMUNE SYSTEM is developing. Breastfeeding, also called nursing, further supports a strong physical and emotional connection between mother and baby.

Though breastfeeding suppresses a woman's normal hormonal cycle to some extent, breastfeeding is not a reliable method of CONTRACEPTION (birth control). It is still possible for a nursing mother to get pregnant.

First Milk: Colostrum

The first milk the mother's breast produces after birth is colostrum, often called premilk. Colostrum is more concentrated than mature breast milk and contains primarily carbohydrate and protein with little fat. This composition is very easy for the infant to digest in the first use of the gastrointestinal system; its concentration delivers more nutrition with less volume. Colostrum also contains a higher concentration of antibodies than mature breast milk. The infant should breastfeed about every two hours in its first few days of life, both to provide sufficient nutrition and to encourage adequate milk production.

Milk Production

The hormones of PREGNANCY establish the initial environment for milk production. The stimulation of the infant's sucking induces the hormonal responses that cause the lactiferous glands of the breasts to produce milk. The lactiferous ducts store some breast milk, though the lactiferous glands actively produce milk as the infant nurses. The breasts will continue producing milk after pregnancy for as long as the baby nurses regularly.

The breast releases mature milk in two surges. The first surge, the foremilk, is thin, bluish, and contains primarily lactose (a simple carbohydrate) and proteins. The second surge, which releases after the infant has nursed for three to five minutes, is hindmilk. Hindmilk is thicker, yellowish, and contains a higher concentration of fats that are essential to supply the infant with a source of energy. The infant may nurse 10 to 30 minutes on hindmilk.

Let the Infant Take the Lead

Lactation and nutrition experts currently recommend that the mother allow the infant to nurse

completely at one breast before switching to the other, even if the infant becomes satiated before switching or before finishing the second breast. The infant generally will pull away from one breast when ready to switch. Following the infant's lead in this way, rather than breastfeeding by the clock, allows the infant to receive maximum nutritional benefit from breastfeeding. Though conventional wisdom has long held that the mother should switch the infant from one breast to the other to provide equal time at each breast under the premise that this practice would to stimulate and sustain the most ideal milk production, recent research suggests the infant may not receive balanced nutrition with such an approach. As well, sucking provides emotional comfort for the infant.

Though breastfeeding is a natural process, the process of breastfeeding does not come naturally for most women. It takes time and patience for the mother to synchronize with the baby's needs and preferences. Birthing centers have lactation specialists who can help new mothers establish effective breastfeeding. New mothers often worry the infant is not receiving enough nourishment. The most accurate measure of this is the infant's steady and appropriate weight gain and development. The breasts seldom drain completely of milk, and the infant may nurse more aggressively at some feedings than others.

Care of the Breasts

The mother's breasts, especially the nipples, are often tender during the first few weeks of breastfeeding. It is important for the infant to latch around a good portion of the areola as well as the nipple when nursing, which properly stimulates the lactiferous glands as well as eases CHAFING and soreness of the nipples. A lactation specialist can help a new mother find the nursing positions that are most effective.

Washing the breasts with warm water after breastfeeding and allowing them to air dry helps prevent irritation and chafing. A nursing bra provides extra support for the breasts, which are quite heavy and enlarged during breastfeeding. Nursing pads inserted inside the bra protect leaking milk from staining clothing. Because many substances pass from the mother's body into the breast milk, the woman should check with her health-care provider before taking over-the-counter (OTC) medications. Certain foods appear to bother some infants, probably altering the taste or smell of the breast milk.

Expressing and Storing Breast Milk

Many women express (pump) milk from their breasts to store for feeding the baby when breastfeeding is not possible, such as after the woman returns to work. This allows other people to use a bottle to feed breast milk to the baby. Expressed breast milk will remain fresh for one week when refrigerated and for four months when frozen. Breast pumps simulate the rhythmic pressure of nursing, initiating the letdown REFLEX and releasing milk. It may take longer to express full breasts when pumping than when the baby nurses, though it is important to get as much milk as possible so milk production remains constant. The breasts adjust how much milk they produce according to the demand for milk.

See also ANTIBODY; BREAST HEALTH; MASTITIS.

breast health Measures a woman can take throughout her life to maintain the best possible health for her breasts. Because there is such wide variation around what is "normal" when it comes to breasts, health experts urge women to become familiar with the appearance and feel of their own breasts so they can easily and quickly detect changes that warrant further medical evaluation. A comprehensive approach combines lifestyle habits that support BREAST health with monthly BREAST SELF-EXAMINATION, regular breast exams from a health-care provider, and MAMMOGRAM (when age appropriate).

A woman's breasts are somewhat dynamic in that they undergo cyclic changes that follow the MENSTRUAL CYCLE. The glandular tissues respond to ESTROGENS and PROGESTERONE in the woman's BLOOD circulation. The same hormonal patterns that prepare the UTERUS for PREGNANCY also prepare the breasts to produce milk. They also cause cyclic changes in the breasts. Many women find their breasts become tender and somewhat swollen during the week before their menstrual periods—the luteal or secretory phase of the menstrual cycle when estrogen levels are especially high.

Women who have fibrocystic breasts may experience increased symptoms during this time. Knowing these cyclic patterns makes it easier to distinguish normal from unusual changes.

Lifestyle factors that influence breast health include EATING HABITS, physical exercise, and cigarette smoking. Some research studies suggest a diet high in saturated fat (animal fat) raises the risk for FIBROCYSTIC BREAST DISEASE and BREAST CANCER. The findings of other studies are inconclusive. There is increased risk for breast cancer with OBESITY, however, which may be a consequence of diet and exercise or a function of increased estrogen in the blood circulation as a result of aromatase conversion of stored estrogen in adipose (fat) cells. Numerous studies associate cigarette smoking with increased risk for fibrocystic breast disease, fibroadenoma (noncancerous breast tumor), breast cancer, and cancer overall.

See also DIET AND HEALTH; EXERCISE AND HEALTH; MASTITIS; OBESITY AND HEALTH; SMOKING AND HEALTH; SMOKING CESSATION.

breast self-examination A method a woman can use to examine her breasts for changes such as lumps and irregularities in the BREAST tissue. The primary purpose of breast self-examination (BSE) is to familiarize a woman with the normal appearance and feel of her breasts so she can detect changes that may warrant medical evaluation. Though most lumps and irregularities a woman detects through BSE are benign (noncancerous), BSE can result in early discovery of BREAST CANCER. The risk for breast cancer increases with age and is highest after MENOPAUSE.

The ideal time to perform BSE is at the end of the menstrual period when the breasts are least sensitive. BSE takes only a few minutes, following these steps:

1. Stand in front of a mirror, unclothed, with arms at the sides. Look at the breasts for any indentations, irregularities, or distortions to the shape of the breast.
2. Raise the arms and repeat the visual examination.
3. With the flat surfaces of the fingers of the left hand, gently feel the right breast starting at the nipple and moving outward in a circular pattern to cover the entire breast. Also feel into the armpit area, which contains breast tissue.
4. Gently squeeze the nipple to detect any discharge.
5. Repeat steps 3 and 4 for the left breast.
6. Lie on the back on a flat surface with the right hand behind the head. Repeat steps 3 and 4.
7. Switch to put the left hand behind head and repeat steps 3 and 4 for the left breast.

Though BSE primarily targets women, it is good preventive health for men to also become familiar with the appearance and feel of their breasts. Breast cancer is rare but can occur in men. Though lumps in the breast are easier to detect in men, men are more likely to disregard them as insignificant. A doctor should evaluate any lump that develops in a man's breast.

See also MAMMOGRAM; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS; TESTICULAR SELF-EXAMINATION.

C

cancer of the penis A malignant (cancerous) tumor that arises from the tissues of the PENIS. Cancer of the penis is rare and usually occurs in men over age 50. Men who are uncircumcised and men who have HUMAN PAPILLOMAVIRUS (HPV) infection have increased risk for cancer of the penis. Early symptoms include a painless growth, bump, or sore at the tip of the penis. In an uncircumcised man such a growth most commonly appears beneath the foreskin, which often delays the cancer's detection. Early diagnosis and treatment allow the least invasive treatment. Surgery is the preferred treatment to remove the cancerous tumor and a safe margin of healthy tissue. Follow-up surgery to reconstruct the penis is sometimes necessary. Depending on how advanced the cancer is, the oncologist may recommend RADIATION THERAPY or CHEMOTHERAPY in addition to surgery.

See also CANCER TREATMENT OPTIONS AND DECISIONS; CIRCUMCISION; METASTASIS; PROSTATE CANCER; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; PLASTIC SURGERY; SURGERY FOR CANCER; TESTICULAR CANCER.

cervical cancer A malignant (cancerous) tumor that originates in a woman's CERVIX. The cervix is a thick neck of tissue that joins the VAGINA and the UTERUS. INFECTION with the HUMAN PAPILLOMAVIRUS (HPV) accounts for nearly all cervical cancer, though only about 15 of the 100 or so strains of HPV are connected with cervical cancer and only a small percentage of women who have HPV infection with one of those strains actually develops cervical cancer.

Cervical cancer tends to follow a predictable path of development that takes many years to evolve, typically 10 years or longer. Because of this, with early detection cervical cancer is one of the most curable forms of cancer. The path of development for cervical cancer begins with slight changes in the cells of cervical tissue, called cervical DYSPLASIA. Though not cancer, dysplasia is a circumstance of irregular cell growth. All cervical cancer begins as cervical dysplasia. Because of this, even though only a small percentage of cervical dysplasia become cancer doctors consider cervical dysplasia a broad classification of cell abnormalities that range from precancerous to cancerous.

Doctors call moderate to severe cervical dysplasia, which is precancerous, CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN). Doctors believe about two thirds of untreated cervical dysplasia progresses to cancer. The PAP TEST, a laboratory examination of cells swabbed from the cervix, can detect cervical dysplasia, CIN, and other changes in cervical tissue. A Pap test is part of a routine PELVIC EXAMINATION.

Symptoms and Diagnostic Path

Cervical cancer often shows no symptoms until it spreads outside the cervix, which is why routine Pap tests are so crucial in its detection. When symptoms are present they may include

- watery, sometimes blood-tinged discharge
- vaginal bleeding between menstrual periods or after MENOPAUSE
- vaginal bleeding during or after SEXUAL INTERCOURSE
- unusually heavy or prolonged menstrual periods
- low back discomfort
- unexplained tiredness, lack of energy, or fatigue
- URINARY URGENCY or URINARY FREQUENCY

The diagnostic path begins with pelvic examination, Pap test, and HPV testing, including HPV DNA. COLPOSCOPY (examination of the cervix with a special lighted microscope) provides additional information about the location and extensiveness of the cancer. Cervical biopsy (laboratory examination of tissue samples taken from the cervix) provides definitive diagnosis. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) may show the extent to which the cancer has metastasized to locations within or distant from the pelvis. The pathologist determines the grade (degree of abnormality of the cells) and stage (extent of the tumor) from the biopsy tissue samples. STAGING AND GRADING OF CANCER is important for determining appropriate CANCER TREATMENT OPTIONS AND DECISIONS.

BASIC STAGING OF CERVICAL CANCER

Stage	Meaning	Treatment Options
cervical intraepithelial neoplasia (CIN2/CIN3)	cells are abnormal but precancerous and confined to a localized area of the CERVIX	cryosurgery, laser surgery, loop electrosurgical procedure (LEEP), or excisional conization to remove abnormal cells frequent and regular PAP TEST and COLPOSCOPY
CIN4/stage 0/carcinoma in situ	cancer remains confined to the cells of its origin	cryosurgery, laser surgery, LEEP, or excisional conization to remove abnormal tissue frequent and regular Pap test and colposcopy
stage 1	cancer remains confined to a small, clearly defined area of the cervix stage 1A is microscopic; stage 1B is barely visible to the unaided eye	stage 1A: total HYSTERECTOMY frequent and regular Pap test and colposcopy stage 1B: modified radical HYSTERECTOMY with SENTINEL LYMPH NODE DISSECTION and adjuvant RADIATION THERAPY and/or CHEMOTHERAPY *or* high-dose external beam radiation combined with internal seeding
stage 2	cancer has spread to other structures within the pelvis but not to distant organs stage 2A involves the upper VAGINA; stage 2B involves parametrial tissue	high-dose external and internal radiation therapy in combination with platinum-agent chemotherapy
stage 3	cancer has spread widely within the pelvis and may involve the lower vagina and ureters stage 3A involves the lower vagina but not the pelvic wall; stage 3B involves the pelvic wall or the pelvic LYMPH nodes	combination chemotherapy palliative radiation therapy clinical trials
stage 4	cancer has spread to distant organs or recurred (come back) after treatment stage 4A involves lower abdominal organs; stage 4B involves distant organs	combination chemotherapy palliative radiation therapy clinical trials

Treatment Options and Outlook

Cervical cancer is almost always curable with minimally invasive treatment when doctors detect it as CIN or stage 1. Stage 2 and stage 3 cervical cancers require more invasive treatments and have lower potential for cure. The primary treatment of choice for most stage 1 cervical cancers is surgery to remove the tumor, the entire cervix, or, in more advanced stages, the cervix and adjacent tissues such as the upper vagina and often the uterus (total or modified radical HYSTERECTOMY). Adjuvant (follow-up) treatment may include CHEMOTHERAPY or RADIATION THERAPY. High-dose radiation therapy (external beam and internal seeding) in combination with chemotherapy, is the primary treatment of choice for most stage 2 and stage 3 cervical cancers as these have usually spread beyond the scope of surgery, though surgery may be an option for stage 2 cervical cancer that remains confined to the upper vagina. The treatment of choice for stage 4 cervical cancer is combination chemotherapy with palliative radiation therapy to relieve symptoms of obstructive tumors.

CHEMOTHERAPY AGENTS TO TREAT CERVICAL CANCER	
carboplatin	cisplatin
gemcitabine	paclitaxel
topotecan	vinorelbine

Risk Factors and Preventive Measures

The key risk factors for cervical cancer are HPV infection with one of the few strains of HPV linked to cervical cancer, multiple sexual partners, and cigarette smoking. The HPV vaccine prevents infection with HPV types 6, 11, 16, and 18, the strains of HPV associated with genital warts and cervical cancer. Health experts recommend HPV vaccination for girls beginning at age 12, though women to age 26 can receive the vaccine. Because HPV accounts for nearly all cervical cancer, measures to reduce exposure to HPV infection (such as condom use and mutual monogamy) are also crucial. Routine pelvic examination with Pap test can detect cervical cancer in its earliest, curable stages.

See also BREAST CANCER; CONTRACEPTION; ENDOMETRIAL CANCER; HIV/AIDS; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SURGERY BENEFIT AND RISK ASSESSMENT.

cervical intraepithelial neoplasia (CIN) The growth of abnormal cells within the tissue of the CERVIX. Because without treatment CIN often progresses in severity and is the foundation of CERVICAL CANCER, doctors consider CIN a precancerous condition and grade it according to the extent to which it infiltrates the cervix. The four grades, or levels of severity, of CIN are

- grade 1, or CIN1, in which the abnormal cells infiltrate only the first layer of tissue; CIN1 often goes away on its own though merits careful observation until it is clear that it has done so
- grade 2, or CIN2, in which the abnormal cells penetrate to the second or third layer of tissue; standard treatment is surgical removal of the affected tissue using the loop electrosurgical excision procedure (LEEP)
- grade 3, or CIN3, in which the abnormal cells penetrate through the third layer of tissue and involve a fairly substantial area of cervical tissue; standard treatment is surgical removal of the affected tissue, usually using LEEP and sometimes using conization
- grade 4, or carcinoma in situ, in which the abnormal cells completely penetrate all epithelial layers using conization

Though CIN often follows an orderly progression from grade 2 to grade 4, culminating with cervical cancer, it does not always do so. About a third of CIN2 and CIN3 progresses to the next level and three fourths of women who have CIN4 or carcinoma in situ eventually develop cervical cancer. However, CIN1 progresses to cervical cancer in only 1 percent of women.

Symptoms and Diagnostic Path

Often a woman has no symptoms of CIN; the doctor detects the condition during routine PELVIC EXAMINATION and PAP TEST. COLPOSCOPY (examination of the cervix with a lighted surgical microscope) can sometimes confirm the diagnosis. However, excisional biopsy (removal of the abnormal area and laboratory examination of the tissue) is the definitive diagnostic procedure.

Treatment Options and Outlook

Standard treatment for CIN is removal of the abnormal cells with follow-up pelvic exam, Pap test, and other pathologic tests. The procedures for removal include

- LEEP, an office procedure in which the gynecologic surgeon inserts a wire loop through the VAGINA to the cervix and removes slices of tissue by sending a mild electrical current through the wire loop; LEEP is the standard treatment for CIN2 and some CIN3
- conization, also called excisional conization or cone biopsy, in which the gynecologic surgeon removes larger areas of tissue with instruments inserted through the vagina; the woman usually undergoes general ANESTHESIA, and the procedure is performed in an operating room

These treatments usually cure the CIN, though doctors recommend regular follow-up Pap tests, colposcopy, and other laboratory tests for up to five years after the initial treatment.

Risk Factors and Preventive Measures

The strongest risk for CIN is INFECTION with HUMAN PAPILLOMAVIRUS (HPV). CIN is more common in women who smoke and in women who have HIV/AIDS. A Pap test can detect CIN in its early, easily treatable stages. Preventive measures include safer sex methods (such as abstinence, condom use, or mutually monogamous sexual relationships) to prevent HPV infection. In 2006 the first vaccine to prevent HPV infection in women became available. The vaccine protects against infection with HPV types 6, 11, 16, and 18, the types associated with genital warts and cervical cancer. Health experts recommend HPV vaccination for girls beginning at age 12, though women to age 26 can receive the vaccine.

See also CANCER TREATMENT OPTIONS AND DECISIONS; CELL STRUCTURE AND FUNCTION; SURGERY BENEFIT AND RISK ASSESSMENT.

cervix The neck of the UTERUS, a thick cuff of muscular tissue about one inch in length that joins the VAGINA to the uterus. A narrow channel through the cervix, the cervical canal, allows menstrual material to leave and SPERM to enter the uterus. The opening of the cervix within the uterus is the internal os; the opening of the cervix within the vagina is the external os. The cervix has the ability to thin and dilate to permit CHILDBIRTH.

HEALTH CONDITIONS THAT MAY AFFECT THE CERVIX

CERVICAL CANCER	cervical DYSPLASIA
cervical erosion	CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN)
cervical polyps	GONORRHEA
CHLAMYDIA INFECTION	incompetent cervix during PREGNANCY
HUMAN PAPILLOMAVIRUS (HPV) infection	
trauma	

For further discussion of the cervix within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also COLPOSCOPY; DILATION AND CURETTAGE (D&C); FALLOPIAN TUBES; GENITAL TRAUMA; HYSTERECTOMY; OVARIES; PAP TEST; PELVIC EXAMINATION.

cesarean section Surgical CHILDBIRTH. In cesarean (spelled caesarean in countries other than the United States) section, the obstetrician makes an incision through the abdominal wall and the wall of the UTERUS to extract the FETUS. Doctors in the United States perform cesarean section, also called c-section, to deliver 90 percent of breech presentations (fetus is bottom down rather than head down in the uterus) and about 25 percent of pregnancies overall. Most cesarean sections are unplanned though nonemergency, performed because of the mother's health status, the size of the baby, or the failure of labor to progress. Emergency cesarean section may be necessary when the fetus is in distress.

Though some women feel disappointed or even dismayed to need cesarean delivery, the outcome of healthy baby and healthy mother is the overarching objective. A woman who feels rushed into surgical delivery should discuss alternatives with her obstetrician. Ideally the woman and the obstetrician have had discussions during the course of PRENATAL CARE about the circumstances under which the obstetrician may recommend cesarean section and are in agreement about them.

COMMON REASONS FOR CESAREAN SECTION

cephalopelvic disproportion	ECLAMPSIA
erratic fetal heartbeat	GENITAL HERPES outbreak
higher order multiples (triplets or more)	known serious BIRTH DEFECTS
	known SPINA BIFIDA
macrosomia (very large baby)	maternal CARDIOVASCULAR DISEASE (CVD)
maternal HIV/AIDS	nonprogressive labor
maternal DIABETES	placenta previa
PLACENTA abruptio	previous CESAREAN SECTION
PREECLAMPSIA	prolapsed UMBILICAL CORD
previous uterine surgery	

Most hospitals allow the woman's partner to be present in the operating room during nonemergency cesarean delivery. The partner must change into sterile clothing (scrubs) and remain outside the sterile field, usually seated beside the woman's head; the delivery team will provide clear and specific instruction for the partner. A draped sheet provides a screen to block the woman's view of the OPERATION as it is taking place. Except in emergency situations when time is crucial, ANESTHESIA is nearly always epidural (injection of the anesthetic DRUG into the space around the SPINAL CORD) or spinal. These forms of anesthesia provide complete PAIN relief for the mother but do not affect the infant. General anesthesia, because the drugs enter the mother's BLOOD circulation, affects the infant and may suppress BREATHING and HEART RATE.

Surgical Procedure

After the anesthesia takes effect, the obstetrician makes an incision through the SKIN and abdominal muscles to expose the uterus, then makes an incision through the wall of the uterus to deliver the baby. The most common incision is the low transverse (also called the bikini cut), running horizontally across the lower abdomen just above the pubic BONE about at the pubic hair line. An alternative incision for rapid delivery is the vertical incision, which extends from the umbilicus (belly button) to just above the pubic bone.

The obstetrician first delivers the baby's head and thoroughly suctions the secretions from the NOSE, MOUTH, and upper THROAT. The pressures and forces of a vaginal delivery would squeeze these secretions from the infant as it passed through the birth canal. Removing the secretions is essential to prepare the airways for breathing. The obstetrician then delivers the rest of the baby and clamps the umbilical cord. The pediatrician examines the baby to assess its breathing and overall health. Often the obstetrician allows the woman's partner to cut the cord and show the baby to the mother. To this point, the cesarean section takes about 10 minutes.

The rest of the cesarean section takes about 40 minutes and consists of delivering the placenta, repairing the incision into the uterus, and repairing the incision through the abdominal muscles and the skin. The anesthesiologist may administer a sedative to help the mother relax and sleep during this part, after which she goes to the recovery unit until the epidural anesthesia wears off and sensation returns.

Risks and Complications

The risk for serious complications is very low with cesarean section. Among them are unusual bleeding, blood clots, and INFECTION in the immediate postoperative period, injury to the BLADDER or ureters, and URINARY TRACT INFECTION (UTI). There is also risk, comparable to that of vaginal birth, of injury to the infant.

The path of recovery is substantially longer for cesarean section than for vaginal birth. Most women spend three to five days in the hospital for initial recovery. The doctor will prescribe ANALGESIC MEDICATIONS to relieve pain that are safe for the woman to take while she is BREASTFEEDING. During the first two weeks at home the woman needs to take care of her incision as the doctor instructs. Full recuperation takes six to eight weeks, during which the woman needs help lifting and caring for the baby. However, walking and other physical activities are necessary and important for HEALING as well as to keep the LUNGS clear and to help prevent blood clots.

Long-term complications are rare and are most likely to occur when the cesarean section was an emergency and the obstetrician made a vertical incision. This incision creates weakness in the abdominal wall, the muscles of which have already stretched as a consequence of the pregnancy. Proper care is essential for optimal healing. The risk of incisional HERNIA is higher with the vertical incision than the transverse incision.

Outlook and Lifestyle Modifications

While the incision is healing the woman needs substantial help carrying and lifting the infant as well as with daily activities. After healing is complete the woman may and should return to full activities, including SEXUAL INTERCOURSE as she desires. Cesarean section does not affect the ability to breastfeed for as long as the woman desires or the potential for becoming pregnant again. Vaginal delivery with subsequent pregnancies (VBAC, or vaginal birth after cesarean) is possible for about two thirds of women who had transverse incisions on the uterus. Most obstetricians consider a vertical incision on the uterus too risky for VBAC because the stress of labor may cause the incisional SCAR on the uterus to rupture.

For further discussion of cesarean section, please see the overview section "The Reproductive System."

See also APGAR SCORE; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

childbirth The passage of the FETUS from the UTERUS to independent life outside the woman's body as PREGNANCY culminates. The physiologic processes that establish this passage are labor and delivery (vaginal birth); childbirth may also occur as a surgical procedure (CESAREAN SECTION). Labor refers to the progressively intense contractions of the uterus that dilate and efface (stretch and thin) the CERVIX, then push the fetus into and through the VAGINA (birth canal).

Though labor and delivery occur in predictable and sequential stages, their timing varies widely. Early labor may last a few to 36 hours. Active labor generally lasts 2 to 8 hours. Delivery, the passage of the baby through the birth canal, may take 15 minutes to 2 hours. A woman's first delivery typically takes longer than subsequent deliveries. Though childbirth is a natural process, in the United States most childbirth takes place in hospitals or birthing centers with medical professionals (doctors, nurses, midwives) providing care and assistance.

Stage 1: Labor

Labor is the work of the uterus and abdominal muscles to ready the woman's body for birth and ultimately push the infant out. For more than 40 weeks the body's focus has been on maintaining the pregnancy within it. As the time for birth approaches, hormonal signals initiate the sequence of events that will make delivery possible. Researchers do not know what starts the hormonal cascade that ultimately results in childbirth, though these changes begin some time before actual labor starts.

Though the most intense experience of labor is in the hours that lead to delivery, the preparations actually begin several weeks before birth. One of the earliest signs of impending birth is the dropping of the presenting part of the fetus, usually the head, into the start of the cervix. Called engagement or lightening, this movement indicates the cervix is beginning to efface. It also signals changes that are occurring within the fetus to prepare it for life outside the womb, notably expansion of the LUNGS.

As the cervix continues to efface and begins to dilate the plug of mucus that formed in the cervical canal comes loose and slides out, which the woman may notice as a brownish discharge (sometimes called bloody show). This may occur a week or longer before birth. The characteristic experience of labor begins with sensations of tightening and relaxing in the lower abdomen, somewhat similar in experience to menstrual cramps. Many women feel these sensations in the lower back as well. The woman may feel restless and want to walk around; walking helps strengthen and coordinate contractions as they progress. Labor becomes more intense and focused when the membranes rupture, often called water breaking.

There are many ways women cope with the discomfort of labor, which intensifies as the labor progresses. Methods such as relaxation BREATHING, massage, acupuncture, and visualization often help a woman feel calm and centered. Some women become intensely active in the early stages of labor, cleaning house and otherwise "nesting." Doctors believe this behavior harkens to primal instincts of preparedness. In early labor contractions may be 10 to 15 minutes apart and last about 30 seconds and may become less intense with certain positions or activities. As early labor progresses to active labor, contractions are about 5 minutes apart and last for 45 to 60 seconds.

In active labor contractions continue to increase in frequency and intensity, and discomfort progresses to PAIN. Many women feel the need for pain relief during active labor. Common methods include narcotic ANALGESIC MEDICATIONS and regional ANESTHESIA such as epidural block. Active labor dilates the cervix to 7 or 8 centimeters.

The final stage of labor is transition, during which contractions come in waves often without more than seconds between them. Transition consumes the woman's attention and focus; she often is not aware of activity taking place around her. Many women feel the urge to push, though should not do so because the cervix is not yet ready. Transition is usually complete within three hours. The cervix finishes dilating to a wide-open 10 centimeters, and birth is imminent.

Stage 2: Delivery of the Baby

Delivery requires much conscious effort from the woman to push with contractions. The birthing team coaches and guides the process. The urge to push may be overwhelming; going with it is usually the most efficient approach unless the doctor or midwife advises to wait. Sometimes the baby's position in the birth canal becomes awkward such that waiting a few moments allows a turn or movement that then responds better to pushing. An epidural for pain relief tends to extend delivery somewhat because the woman does not as strongly feel the urge to push.

The head emerges first, with the shoulders and then the rest of the body following. The doctor or midwife suctions any mucus and BLOOD from the baby's NOSE and MOUTH. The baby begins breathing as soon as his or her body clears the birth canal and the chest can expand. When all is well, the doctor or midwife places the baby on the mother's chest for her to hold and clamps the UMBILICAL CORD in two places. The partner, the mother, an older sibling present for the birth, or the birthing attendant may cut between the clamps to sever the cord.

Stage 3: Delivery of the Placenta

After a brief pause contractions resume to separate the PLACENTA from the endometrium and push it from the body. It takes about 10 minutes to deliver the placenta, which sometimes requires the woman to bear down to help push it out. The uterus then continues mild contractions, which are important to restore its firmness and to stop bleeding. A member of the birthing team may massage the mother's lower abdomen to further stimulate these contractions. BREASTFEEDING the infant at this time is also helpful because the sucking at the BREAST releases OXYTOCIN, a HORMONE that continues the uterine contractions as well as releases colostrum (premilk) for the infant.

For further discussion of childbirth, please see the overview section "The Reproductive System."

See also POSTPARTUM DEPRESSION; PRENATAL CARE; VBAC.

chordee A congenital (present at birth) downward curvature of the PENIS. Chordee results from extra connective tissue that contracts the ventral surface of the penis, pulling the tip of the penis downward. Chordee typically occurs in conjunction with HYPOSPADIAS, a CONGENITAL ANOMALY in which the opening of the URETHRA (the meatus) is on the underside of the penis rather than at the tip. Chordee may be apparent only during ERECTION or may contract the penis significantly enough to prevent normal URINATION. Mild chordee that does not interfere with urination or SEXUAL INTERCOURSE does not require treatment. For more severe chordee, surgery to release the connective tissue and, if necessary, to correct the hypospadias relieves the curvature.

See also CIRCUMCISION; PEYRONIE'S DISEASE; PHIMOSIS; SURGERY BENEFIT AND RISK ASSESSMENT.

chorionic villi sampling (CVS) A diagnostic procedure, also called chorionic villus sampling, in which the obstetrician removes small clusters of cells from the hairlike edges of the PLACENTA, the chorionic villi, during PREGNANCY. The cells in this sample provide genetic information about the FETUS that can rule out or diagnose GENETIC DISORDERS such as CYSTIC FIBROSIS and TAY-SACHS DISEASE, NEURAL TUBE DEFECTS such as SPINA BIFIDA, or CHROMOSOMAL DISORDERS such as DOWN SYNDROME. The obstetrician can perform CVS in the first trimester, usually around the 11th week, providing information about potential health concerns early in the pregnancy to allow the woman and her partner to consider possible treatment options as well as

whether, with severe disorders or deformities, to continue the pregnancy.

To withdraw the sample of cells the obstetrician may insert a needle through the abdominal wall and into the UTERUS, similar to AMNIOCENTESIS, or may guide a very small catheter through the VAGINA and CERVIX into the uterus. The obstetrician first numbs either the site on the abdomen or the cervix with a local anesthetic, then uses ULTRASOUND to help place the needle or the catheter. After the procedure the woman may feel mild cramping or experience slight bleeding, which are the main risks associated with CVS. Rarely CVS can cause spontaneous ABORTION (loss of the pregnancy), though the risk with CVS less than the risk with amniocentesis, another prenatal diagnostic procedure, because CVS does not require penetration of the amniotic sac.

The findings available through CVS are not always as definitive as the results of amniocentesis. The advantages of CVS over amniocentesis, however, are twofold. First, the obstetrician can conduct CVS in the first trimester though cannot perform amniocentesis until well into the second trimester. Second, the risk for complications, including injury to the fetus and spontaneous abortion, is lower with CVS. It is important to discuss and thoroughly understand the reasons for either procedure.

See also ALPHA FETOPROTEIN (AFP); CONGENITAL ANOMALY; PRENATAL CARE.

circumcision The surgical removal of the foreskin (prepuce), the thin hood of SKIN that covers the end of the PENIS. The reason for circumcision may be therapeutic, religious, ceremonial, hygienic, cultural, or social. About two thirds of newborn boys in the United States are circumcised shortly after birth for nontherapeutic reasons. Nontherapeutic circumcision should take place within three weeks of birth when done in infancy. Circumcision at an older age, and particularly in adulthood, becomes a more significant surgical procedure with increased risk for complications.

Infant (Neonatal) Circumcision

For infant circumcision, the doctor applies an anesthetic cream or injects a local anesthetic to numb the penis, then applies a circumcision clamp and cuts away the end of the foreskin. The procedure takes about 10 minutes. Some methods leave a plastic ring around the penis that seals the edge of the wound; the ring falls off when the wound heals (within 7 to 10 days). There are no sutures (stitches). Minor bleeding for a day or so after the procedure is common.

Adult Circumcision

Adult circumcision is a minor surgery OPERATION generally performed in a hospital operating room or an AMBULATORY SURGERY FACILITY; it requires regional anesthesia (anesthetic injected into the NERVE that serves the penis) and a general sedative. The circumcision operation takes about 30 minutes; typically a urologist performs the operation. Sutures remain in place for five to seven days after the operation. It is important to try to avoid erections and sexual activity for four to six weeks to allow the surgical wound to heal properly. There is often mild to moderate discomfort during HEALING; the doctor may prescribe or recommend ANALGESIC MEDICATIONS for PAIN relief.

Risks and Complications

Risks associated with circumcision include excessive bleeding, injury to the penis, too much or too little foreskin removed, and postoperative INFECTION. Infants who have a CONGENITAL ANOMALY of the penis such as HYPOSPADIAS or CHORDEE should not undergo circumcision. Health conditions for which circumcision is therapeutic include PHIMOSIS and PARAPHIMOSIS, conditions in which the foreskin does not properly retract or return to its normal position, and chronic or persistent BALANITIS (an infection of the glans that develops under the foreskin).

Medical Debate about Routine Infant Circumcision

Despite its frequency, routine infant circumcision is a matter of considerable debate among health professionals. In 1999 the American Academy of Pediatrics issued a position statement that there are no medical or health reasons for routine circumcision of newborns. Numerous studies have attempted to determine whether circumcision provides health benefits. The findings are mostly inconclusive, with the exception of a significantly increased risk in uncircumcised boys for URINARY

TRACT INFECTION (UTI) during early childhood. Uncircumcised men are more likely to acquire infections such as balanitis and perhaps SEXUALLY TRANSMITTED DISEASES (STDS) such as HUMAN PAPILLOMAVIRUS (HPV) and HIV/AIDS. Circumcision does not provide protection against such infections, however.

See also CANCER OF THE PENIS; CULTURAL AND ETHNIC HEALTH CARE PERSPECTIVES; SURGERY BENEFIT AND RISK ASSESSMENT.

clitoris An organ of the female GENITALIA, located at and partially beneath the junction of the upper folds of the labia. Made of erectile tissue and nerves, the clitoris arises from the same embryonic cells as the male PENIS and, though much smaller, contains parallel structures. Two fused corpora cavernosa (spongy, tubelike channels) form the body of the clitoris, which is about an inch long. During sexual arousal the corpora cavernosa engorge with BLOOD and cause the clitoris to enlarge and become erect. At the end of the clitoris is a small bulb of highly sensitive NERVE tissue, the glans. A thin sheath, the prepuce (analgous to the male foreskin), covers the clitoral glans except during sexual stimulation when it retracts to expose the glans. The only known purpose of the clitoris is sexual stimulation, which increases vaginal lubrication and other physiologic changes to facilitate penetration during SEXUAL INTERCOURSE.

See also ERECTION; GENITAL TRAUMA; SEXUALITY.

colposcopy A diagnostic procedure in which the gynecologist examines a woman's external GENITALIA and the interior VAGINA using a lighted magnifying instrument called a colposcope. The gynecologist may also visualize the CERVIX though the colposcope remains outside the vagina. The colposcope allows the gynecologist to more closely examine the surface of the genital tissues when a PELVIC EXAMINATION or a PAP TEST reveals possible abnormalities. Colposcopy helps the gynecologist determine whether biopsy (removing a small sample of tissue) or another diagnostic procedure is necessary. The gynecologist performs colposcopy as an office procedure that requires no special preparation or anesthetic. Most women find colposcopy no more uncomfortable than a routine PELVIC EXAMINATION though any associated biopsy may cause minor discomfort and slight bleeding for a day or two after the biopsy. There are no aftereffects or risks for complication with colposcopy alone.

See also HYSTEROSCOPY.

conception The culmination of fertilization (union of a SPERM and an ovum) and implantation of the resulting blastocyst into the endometrium (lining of the UTERUS). Conception marks the onset of PREGNANCY.

Numerous factors, internal and external, influence conception. Internal factors include a woman's HORMONE levels and OVULATION patterns, the viability of the man's sperm, and circumstances that occlude the FALLOPIAN TUBES to keep sperm and ovum from meeting, such as scarring from PELVIC INFLAMMATORY DISEASE (PID). External factors that influence conception include cigarette smoking and birth control methods intended to block conception, such as condoms, the intrauterine device, and oral contraceptives (birth control pills).

Health conditions such as ENDOMETRIOSIS and UTERINE FIBROIDS may prevent the pregnancy from proceeding after implantation takes place, resulting in early spontaneous ABORTION (commonly called miscarriage) often before the woman realizes she has conceived.

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); CONTRACEPTION; FAMILY PLANNING; FERTILITY; INFERTILITY; OVA; ZYGOTE.

contraception Any of various methods, also called birth control, intended to prevent PREGNANCY. Contraception allows sexually active women and their partners to prevent as well as plan pregnancies.

The US Food and Drug Administration (FDA) approved the first oral contraceptive in 1960. Thirteen years later the US Supreme Court legalized elective ABORTION. Though they remain controversial even today, these two events were pivotal in the arena of reproductive choice and planning because they were the first methods that placed contraception in the control of women. Now, nearly all forms of contraception are for the woman's use.

COMMON METHODS OF CONTRACEPTION

Method	Male or Female	Availability	Ease of Use	Effectiveness When Used Correctly
cervical cap	female	prescription only; health-care provider must measure and fit	must insert before SEXUAL INTERCOURSE must use with spermicide must remove after specified time	85 percent when woman has not had vaginal CHILDBIRTH 70 percent when woman has had vaginal childbirth
cervical shield	female	prescription only	must insert before sexual intercourse must use with spermicide must remove after specified time	85 percent
condom	male most common; female available	over the counter (OTC)	must put on before each sexual act must withdraw from partner and remove condom for disposal while PENIS remains erect female condom may be difficult to insert	male condom: 85 to 98 percent female condom: 80 to 95 percent
continuous abstinence	both	personal commitment	challenging	100 percent
contraceptive patch	female	prescription only	woman applies once a month	99.9 percent
contraceptive ring	female	prescription only	woman inserts during MENSTRUATION, leaves in place 3 weeks, then removes	98 percent
contraceptive sponge	female	OTC	must insert before sexual intercourse must remove after specified time	65 to 90 percent
depot medroxyprogesterone acetate (DMPA) injection	female	prescription only; health-care provider must administer	received every 12 weeks	99.9 percent
diaphragm	female	prescription only; health-care provider must measure and fit	must insert before sexual intercourse must use with spermicide must remove after specified time	85 to 94 percent

Method	Male or Female	Availability	Ease of Use	Effectiveness When Used Correctly
fertility awareness methods (FAMs)	both	personal commitment	requires diligent effort from both partners	75 to 99 percent
intrauterine device (IUD)	female	prescription only; health-care provider must insert	requires no attention once inserted can stay in the UTERUS for 5 to 12 years, depending on type	99 percent
oral contraceptives	female	prescription only	daily or weekly pill	99 percent
spermicide	female	OTC	must apply before each sexual act	70 to 85 percent
tubal ligation	female	requires surgery	requires no effort after OPERATION permanent	nearly 100 percent (1 in 300 failure rate)
vasectomy	male	requires in-office operative procedure	requires no effort after operation permanent	nearly 100 percent (1 in 500 failure rate)

Common forms of contraception include barrier methods, hormonal methods, mechanical methods, chemical methods, surgical methods, timing methods, and continuous abstinence. Some methods, such as oral contraceptives (birth control pills) and diaphragms, require a doctor's prescription. Others are invasive, such as intrauterine devices (IUDs), TUBAL LIGATION, and VASECTOMY. Still other methods of contraception are available for purchase without prescription or physician approval, sold in locations from grocery and drugstores to dispenser machines in public bathrooms. Most public health departments freely hand out over-the-counter (OTC) methods of contraception, notably condoms.

Contraceptive effectiveness relies primarily on proper use of the method and varies widely among methods as well as within a particular method. The most reliable methods of contraception are those that are in place or effective without any effort at the time of sexual activity. Methods that have the ability to provide nearly 100 percent prevention of pregnancy may actually result in much lower prevention when not used properly. Only about 40 percent of women take oral contraceptives precisely as the label instructions direct, for example, raising the risk for unintended pregnancy.

Many people combine methods to optimize protection from pregnancy, for example using barrier contraception (condom or diaphragm) with chemical methods (spermicides). Only condoms (male or female) also provide protection against SEXUALLY TRANSMITTED DISEASES (STDS). A woman who takes oral contraceptives to prevent pregnancy but has more than one sexual partner also needs the protection of a condom. Partners also should wear condoms for sexual activity during outbreaks of GENITAL HERPES and if they are HIV positive or have HUMAN PAPILLOMAVIRUS (HPV) or HEPATITIS B or C.

Emergency contraception is available through pharmacies in the United States without a doctor's prescription. Emergency contraception, also called the "morning after pill," is a high DOSE of an oral contraceptive. The hormones in the medication

alter the environment within the UTERUS such that a fertilized ovum (egg) cannot implant. The woman must take emergency contraception no later than 72 hours after unprotected SEXUAL INTERCOURSE.

See also CONCEPTION; FAMILY PLANNING; FERTILITY; INFERTILITY; OVA; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SPERM.

cryptorchidism Undescended testicle. The TESTICLES form within the abdominal cavity early in fetal development and normally descend through the inguinal canal at the floor of the pelvis into the SCROTUM during the third trimester of PREGNANCY. In some boys the testicle may spontaneously descend during the first year of life; after one year of age, however, this is unlikely. Numerous factors contribute to cryptorchidism, key among them being genetic and hormonal influences.

Treatment to bring the testicle outside the body is essential to preserve FERTILITY and because a testicle retained within the abdominal cavity has a high risk for TESTICULAR CANCER.

Treatment options are hormonal therapy, in which GONADOTROPIN-RELEASING HORMONE (GNRH) administration may stimulate the testicle to descend on its own, and surgery (ORCHIOPEXY) to shift the testicle from its abdominal position into the scrotum. Orchiopexy is the more common therapeutic route. Surgery sometimes involves procedures to repair related structures such as the arteries and veins that supply the testicle and the VAS DEFERENS, the tubular structure that transports SPERM from the testicle. Bilateral cryptorchism, in which both testicles are undescended, often results in sterility (permanent inability to father a child) because normal body temperature destroys the ability of the testicle to produce sperm.

Even after treatment the risk for testicular cancer remains higher than normal; boys and men who have had cryptorchidism should perform monthly TESTICULAR SELF-EXAMINATION. Most men who had successful treatment for cryptorchidism early in childhood have full fertility. Cryptorchidism does not affect sexual function.

See also FERTILITY; HYPOGONADISM; HYPOSPADIAS; SURGERY BENEFIT AND RISK ASSESSMENT.

D

dilation and curettage (D&C) A surgical procedure, also called dilatation and curettage, in which the gynecologist widens the opening of the CERVIX enough to allow passage into the UTERUS of a narrow scraping instrument called a curette. The gynecologist uses the curette to gently scrape the inside wall of the uterus, removing accumulated BLOOD and tissue that may be causing DYSFUNCTIONAL UTERINE BLEEDING (DUB) or that remains after a spontaneous ABORTION (miscarriage) or an induced abortion using abortifacients (drugs that terminate PREGNANCY).

The doctor performs a D&C in a hospital operating room or AMBULATORY SURGICAL FACILITY with the woman under general ANESTHESIA. The procedure itself takes about 15 minutes; most women are able to go home a few hours after, when they have completely emerged from the effects of the anesthesia. Discomfort similar to moderate menstrual cramps and mild bleeding may occur for up to two weeks after the D&C. Uncommon complications include unusual bleeding during or after the procedure, postoperative INFECTION, and uterine perforation, in which the curette penetrates the wall of the uterus (a small wound that typically heals without intervention). Most women are able to return to normal activities (except SEXUAL INTERCOURSE) within a few days though may feel discomfort for up to a week.

Before undergoing a D&C, a woman should confirm with her gynecologist that the benefits of the procedure outweigh the discomfort and potential complications compared to noninvasive procedures such as ULTRASOUND for diagnostic purposes or medications to treat DUB. Minimally invasive procedures such as endometrial sampling (in which the gynecologist inserts a very thin catheter through the cervix, without dilation, and into the uterus to withdraw a small sample of tissue from the uterine wall) and HYSTEROSCOPY often can provide the same diagnostic information as would D&C but with less risk and discomfort for the woman.

See also SURGERY BENEFIT AND RISK ASSESSMENT.

dysfunctional uterine bleeding (DUB) Bleeding from the UTERUS through the VAGINA that occurs outside the hormonal bleeding normally associated with the MENSTRUAL CYCLE. Doctors believe DUB results from an imbalance between ESTROGENS and PROGESTERONE, the hormones that regulate the menstrual cycle, which allows the endometrium (lining of the uterus) to grow unchecked. The excess tissue dies and sloughs away, producing clotty bleeding.

Vaginal bleeding that saturates more than eight pads in 24 hours for longer than two days may signal a health concern other than DUB and requires prompt medical evaluation.

Symptoms and Diagnostic Path

Because there are numerous causes for abnormal vaginal bleeding, DUB is a diagnosis of exclusion: The doctor concludes the situation is one of DUB after ruling out other possible causes for the bleeding. The essential symptom of DUB is excessive vaginal bleeding. Though the bleeding often has the characteristics of a heavy menstrual period, it may not follow the timing of the woman's menstrual cycle. Some women experience DUB as episodes of bleeding that occur between menstrual periods and for other women the bleeding may be fairly constant or occur with no predictable pattern. Further symptoms of DUB

may include HOT FLASHES and mood swings. Cramping and PAIN are uncommon; these symptoms suggest a diagnosis other than DUB.

Because doctors consider DUB as a diagnosis of exclusion—that is, a diagnosis the doctor reaches after ruling out other possible causes for the bleeding—the diagnostic path may include tests for SEXUALLY TRANSMITTED DISEASES (STDS), BLOOD test to check for PREGNANCY, and other blood tests to measure estrogen, progesterone, and LUTEINIZING HORMONE (LH). A key factor in establishing the diagnosis of DUB is the absence of OVULATION, which characterizes most DUB. The doctor may also check other HORMONE blood levels such as thyroid hormones.

Treatment Options and Outlook

For most women the first course of treatment for DUB is HORMONE THERAPY to restore the body's natural estrogen–progesterone balance. For women of childbearing age this might mean oral contraceptives (birth control pills); for women near MENOPAUSE this might mean a hormone medication such as conjugated estrogens with progesterone or progesterone supplementation. The general therapeutic approach is to take hormone therapy until the menstrual cycle returns to normal, typically three to six months. Nonhormonal medications that may relieve mild DUB include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). Because long-term excessive bleeding commonly results in iron-deficiency ANEMIA, the doctor may also prescribe an iron supplement.

When the medication path is not sufficient, the gynecologist may choose to perform endometrial ablation, in which the gynecologist uses electrocautery, hot balloon, or surgical laser to burn away the endometrial lining and the thin layer of uterine tissue beneath it. This restores the inside of the uterus to its base level so it can resume its natural cycle of thickening and sloughing. Other surgical options include DILATION AND CURETTAGE (D&C), to gently scrap away the endometrial lining, and HYSTERECTOMY (removal of the uterus). Though DUB is one of the most common reasons for hysterectomy, hysterectomy is generally the treatment of final choice for DUB, the treatment gynecologists turn to when other treatment options are not practical or are not successful. Because hysterectomy is a major surgery with numerous potential risks and permanently ends a woman's ability to become pregnant, it is an option that requires careful consideration.

Risk Factors and Preventive Measures

DUB occurs most often during the first and last years of the menstrual cycle. Progesterone-only methods of CONTRACEPTION may also precipitate DUB. However, there are no known measures for preventing DUB.

See also AMENORRHEA; DYSMENORRHEA; ECTOPIC PREGNANCY; ENDOMETRIAL HYPERPLASIA; HYPERTHYROIDISM; HYPOTHYROIDISM; MENSTRUATION; POLYCYSTIC OVARY DISEASE (PCOD).

dysmenorrhea Cramping, PAIN, abdominal bloating, and other discomforts associated with MENSTRUATION. Primary dysmenorrhea occurs without underlying health conditions that cause such symptoms and generally begins within two or three years of MENARCHE (the onset of menstruation). Secondary dysmenorrhea occurs because of underlying health conditions such as ENDOMETRIOSIS or UTERINE FIBROIDS and typically begins later in a woman's life as these conditions develop. Congenital anomalies that affect the way menstrual material flows from the body may also cause secondary dysmenorrhea that is present from menarche.

Doctors believe primary dysmenorrhea, which is the more common form of dysmenorrhea, results from the combination of hormonal actions that reduce BLOOD flow to the endometrium (lining of the UTERUS that thickens in the first half of the MENSTRUAL CYCLE to prepare the uterus for possible PREGNANCY) and initiate menstruation. As the body's balance of estrogen and progesterone shifts, the uterus releases PROSTAGLANDINS and vasopressin. These hormones cause the smooth MUSCLE tissue of the uterus to contract, helping expel the sloughed endometrial tissue that forms the menstrual discharge. Prostaglandins also play a key role in INFLAMMATION and sensitize NERVE endings to pain signals.

Symptoms and Diagnostic Path

Dysmenorrhea presents a characteristic spectrum of symptoms that occur in varying degrees among

different women though are usually consistent from period to period in an individual woman. These symptoms may include

- crampy pain in the lower abdomen, often extending into the lower back and sometimes occurring in a combination of steady cramps with intermittent spasms or outright pain
- sensation of heaviness in the lower abdomen
- bloating (fluid retention)
- HEADACHE
- NAUSEA and VOMITING
- bowel disturbances (CONSTIPATION or DIARRHEA)
- fatigue

Symptoms often vary in severity over the course of the menstrual period, typically being more severe during the first two to three days of menstrual bleeding. About 10 percent of women who have dysmenorrhea have symptoms severe enough to prevent their participation in regular daily activities. The diagnostic path begins with a medical examination that includes a comprehensive health history (including history of sexual activity), PELVIC EXAMINATION, PAP TEST, and laboratory tests for SEXUALLY TRANSMITTED DISEASES (STDS). Any abnormal findings suggest secondary dysmenorrhea and require additional assessment and appropriate diagnostic procedures. Normal findings establish a presumed diagnosis of primary dysmenorrhea.

Treatment Options and Outlook

Medications are the first choice of treatment for primary dysmenorrhea. Those that provide the greatest level of relief are NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which block the release of prostaglandins, and oral contraceptives (birth control pills), which regulate the estrogen–progesterone balance as well as reduce prostaglandin release. Some women obtain adequate relief from over-the-counter NSAIDs; other women require stronger prescription NSAIDs. For severe dysmenorrhea that does not improve with these treatments, the gynecologist may recommend extended cycle oral contraceptives, a therapy that reduces the frequency of menstrual periods to every three months, or HORMONE THERAPY to suppress menstruation up to 12 months. Lifestyle and complementary methods for relief of symptoms include ACUPUNCTURE, thiamine supplementation, herbal therapies, dietary changes to decrease inflammation, heat to the lower abdomen or back, progesterone cream, and daily physical exercise. Treatment for secondary dysmenorrhea targets the underlying condition as well as symptom relief.

MEDICATIONS TO TREAT DYSMENORRHEA

diclofenac	ethinyl estradiol and norethindrone
ethinyl estradiol and norgestimate	ibuprofen
ketoprofen	meclofenamate
mefenamic acid	naproxen

Risk Factors and Preventive Measures

Menstrual cramps and associated discomforts are very common among menstruating women. Women who have a heavy menstrual flow, who have not carried a pregnancy to term, or who smoke cigarettes are more likely to have dysmenorrhea. Physical inactivity, OBESITY, and chronic PELVIC INFLAMMATORY DISEASE (PID) may also influence dysmenorrhea. Health conditions that may exacerbate dysmenorrhea include DYSFUNCTIONAL UTERINE BLEEDING (DUB), endometriosis, and uterine fibroids. Because dysmenorrhea occurs only among menstruating women, the end of menstruation brings the end of dysmenorrhea. Circumstances that end menstruation include MENOPAUSE (the natural cessation of the menstrual cycle that occurs with aging), HYSTERECTOMY (surgical removal of the uterus), and some treatments for cancer such as CHEMOTHERAPY or RADIATION THERAPY to the abdomen.

See also AMENORRHEA; CONTRACEPTION; EXERCISE AND HEALTH; HYPERTHYROIDISM; HYPOTHYROIDISM; PREMENSTRUAL SYNDROME (PMS); SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SMOKING AND HEALTH.

E

eclampsia A potentially life-threatening complication of PREGNANCY in which the woman experiences tonic–clonic seizures, extreme HYPERTENSION (high BLOOD PRESSURE), and periods of unconsciousness or COMA. Eclampsia threatens the well-being of the FETUS because it so dramatically affects the mother's health that prompt delivery is usually necessary, risking preterm birth when eclampsia occurs before 37 weeks gestation.

Routine PRENATAL CARE, which allows early detection of problems such as hypertension in the pregnancy, and aggressive treatment for PREECLAMPSIA, which is often though not always the precipitating condition, make eclampsia relatively uncommon in the United States. When it does occur, eclampsia usually develops between the 20th week of pregnancy and the first week after CHILDBIRTH (though sometimes occurs up to several weeks later).

Doctors do not know what causes eclampsia or what causes some women who have preeclampsia (sometimes called toxemia of pregnancy or gestational hypertension) to progress to eclampsia and others not. The treatment of choice for eclampsia is intravenous magnesium sulfate to stop the seizures with delivery of the baby as rapidly as possible. When eclampsia occurs before fetal viability (generally 24 weeks), doctors may attempt to control the hypertension and seizures in the mother to allow the fetus to further mature. However, the best outcomes for mother and baby occur with the earliest intervention possible. There are no known measures to prevent eclampsia.

See also GESTATIONAL DIABETES; SEIZURE DISORDERS.

ectopic pregnancy A life-threatening circumstance in which a fertilized ovum (ZYGOTE) implants in a location outside the UTERUS, usually in one of the FALLOPIAN TUBES though sometimes elsewhere in the abdominal cavity. A woman's body cannot support such a PREGNANCY; if an ectopic pregnancy continues beyond the very early stages of development it will cause the structure supporting (such as the fallopian tube) it to rupture. The resulting hemorrhage (uncontrolled bleeding) becomes life-threatening without treatment.

Symptoms and Diagnostic Path

Early symptoms of ectopic pregnancy typically occur before the woman realizes she may be pregnant and mimic those of the onset of MENSTRUATION. They may include

- cramping in the lower abdomen
- aching or PAIN in the lower back
- NAUSEA
- slight vaginal bleeding (spotting)

Many women do not experience early symptoms, however. The symptoms of ectopic pregnancy rapidly worsen, often over a period of hours, progressing to sharp pain in the lower abdomen and often shock and loss of CONSCIOUSNESS. Bleeding is usually internal, into the abdominal cavity, and consequently not apparent. The diagnostic path typically includes PELVIC EXAMINATION, BLOOD test for pregnancy, and abdominal ULTRASOUND. The ultrasound can detect abnormal tissues and bleeding.

Emergency medical care is essential for symptoms of ectopic pregnancy. Ectopic pregnancy cannot survive and is life-threatening for the woman.

Treatment Options and Outlook

Abortifacient medications (drugs that cause ABORTION, or loss of a pregnancy) such as methotrexate may terminate an ectopic pregnancy detected very early, avoiding the need for surgery and minimizing the risk for damage to the fallopian tubes and other structures. Such medications work by stopping cell division, affecting rapidly dividing cells such as those of the zygote. These medications were first developed, and are still used, to treat cancer, in which cells also rapidly divide.

Ectopic pregnancy that becomes at all advanced requires surgery that terminates the pregnancy and removes the tissues that have developed to support it. There may be damage to the structure where the pregnancy implanted, such as the fallopian tube or less commonly the CERVIX or ovary, that requires surgical repair. With prompt treatment most women recover fully from ectopic pregnancy though the experience of an ectopic pregnancy is often emotionally traumatic because the pregnancy cannot survive. Damage to or loss of the involved fallopian tube or ovary, if it occurs, may subsequently impair FERTILITY.

Risk Factors and Preventive Measures

Ectopic pregnancy occurs when there is a mechanical or hormonal impediment that prevents or slows the zygote's movement through the fallopian tube to the uterus after fertilization as is the normal process in establishing pregnancy. Risk factors for ectopic pregnancy include

- PELVIC INFLAMMATORY DISEASE (PID), which often results in scarring and blockage of the fallopian tubes
- congenital abnormalities of the fallopian tubes
- progesterone-only contraceptives, which work by impeding the implantation process
- TUBAL LIGATION in which the fallopian tube partially reopens and allows SPERM to escape into the abdominal cavity, or surgical reversal of tubal ligation to restore fertility
- use of an intrauterine device (IUD) for contraception
- ENDOMETRIOSIS
- abdominal adhesions (SCAR tissue), resulting from abdominal surgery such as APPENDECTOMY, that pull the fallopian tubes out of their normal positions
- previous ectopic pregnancy

Though there are no measures to prevent ectopic pregnancy, prompt medical attention to early symptoms of ectopic pregnancy allows treatment before life-threatening complications arise. Early treatment also helps preserve fertility.

See also CHEMOTHERAPY; CONTRACEPTION; OVA.

ejaculation The forceful contractions that expel SEMEN from the erect PENIS during the male ORGASM. Though ejaculation occurs as a result of sexual stimulation, the muscular contractions that produce ejaculation are not within voluntary control. Ejaculation moves semen (SPERM and seminal fluid) from the seminal vesicles, VAS DEFERENS, and PROSTATE GLAND into the URETHRA, and then ejects it from the urethra. In a man who has had a VASECTOMY, the semen does not contain sperm. A tiny valve at the urethral entrance to the BLADDER closes across the bladder opening, directing the flow of semen through the urethra to the outside of the penis. In a man who has had a PROSTATECTOMY (surgery to remove the prostate gland), ejaculation is retrograde (the semen enters the bladder instead of exiting through the urethra) because the OPERATION also involves removal of this valve.

For further discussion of ejaculation within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also RETROGRADE EJACULATION.

embryo The stage of prebirth development from the 15th day after CONCEPTION to 8 weeks of gestational age. The embryo arises from the three germ layers of the ZYGOTE:

- The ectoderm is the outermost layer. It is the foundation for the SKIN and mucous membranes, the TEETH, and the structures of the nervous system.
- The mesoderm is the middle layer. It is the foundation for the organs and structures of the musculoskeletal, cardiovascular, pulmonary,

gastrointestinal, urinary, and reproductive systems.

- The endoderm is the innermost layer. It is the foundation for the tissues that line the inside of the gastrointestinal, urinary, pulmonary, and reproductive organs and structures.

These layers differentiate into their respective structures and organs during the embryonic stage. When this differentiation is complete, the developing life becomes a FETUS.

For further discussion of the embryo within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also PREGNANCY.

endometrial cancer A malignant (cancerous) tumor, sometimes called uterine cancer, that arises from the tissues of the endometrium, the lining of the UTERUS. Often endometrial cancer is HORMONE driven, which means it requires ESTROGENS to grow. Doctors in the United States diagnose endometrial cancer in about 40,000 women each year; it is the fourth most common cancer among women. With early detection and treatment, endometrial cancer is highly treatable. Endometrial cancer tends to develop slowly, typically over years, and most commonly occurs in women over age 60.

Endometrial cancer develops when the cells that form the endometrium become disordered, often as a consequence of chronic ENDOMETRIAL

BASIC STAGING OF ENDOMETRIAL CANCER

Stage	Meaning	Treatment Options
stage 0/carcinoma in situ	cancer remains confined to the cells of its origin	total HYSTERECTOMY with optional bilateral salpingo-OOPHORECTOMY
stage 1	cancer remains confined to the body of the UTERUS	total hysterectomy with bilateral salpingo-oophorectomy and SENTINEL LYMPH NODE DISSECTION adjuvant RADIATION THERAPY
stage 2	cancer involves the uterus and the CERVIX	preoperative radiation therapy total hysterectomy with bilateral salpingo-oophorectomy and sentinel lymph node dissection
stage 3	cancer has spread beyond the uterus though remains confined to the pelvic area cancer may involve the VAGINA and LYMPH nodes adjacent to the uterus	preoperative radiation therapy radical hysterectomy adjuvant HORMONAL THERAPY
stage 4	cancer has spread to other organs in the abdomen such as the RECTUM or BLADDER cancer has spread to distant sites	radiation therapy hormonal therapy clinical trials
stage 4 recurrent	cancer has returned after treatment	radiation therapy hormonal therapy clinical trials four to six cycles of two-drug (doxorubicin and cisplatin) or three-drug (doxorubicin, cisplatin, and paclitaxel) combination CHEMOTHERAPY IMMUNOTHERAPY

HYPERPLASIA (overgrowth of the endometrium). Endometrial hyperplasia occurs when there is an imbalance between estrogens and PROGESTERONE in the woman's BLOOD circulation. Researchers do not know what sets the stage for this imbalance. Elevated estrogens cause the endometrium to thicken and engorge with blood, and diminished progesterone fails to initiate adequate sloughing of the endometrial tissue (such as during MENSTRUATION). The tissue continues to accumulate, and over time its cells become abnormal.

Symptoms and Diagnostic Path

Because endometrial cancer usually develops later in life, its symptoms sometimes blend with those of MENOPAUSE. Because of this a doctor should evaluate symptoms that persist, even when the symptoms do not seem especially serious. Early symptoms of endometrial cancer include

- unusually long or severe menstrual periods
- spotting or bleeding between menstrual periods
- watery, blood-tinged vaginal discharge
- PAIN during SEXUAL INTERCOURSE
- pelvic or lower abdominal pain

The diagnostic path includes a comprehensive medical examination with PELVIC EXAMINATION, during which the doctor often can palpate (feel) a growth within the uterus or detect abnormalities in the uterus's size or shape. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or ULTRASOUND may provide further information. However, only endometrial biopsy can provide a certain diagnosis. The doctor may obtain a tissue sample for biopsy by inserting a narrow catheter through the VAGINA and CERVIX into the uterus and aspirating (suctioning) cells from the endometrium. HYSTEROSCOPY or the surgical OPERATION DILATION AND CURETTAGE (D&C) may also provide endometrial cells for pathology analysis.

When confirming the diagnosis, the pathologist assigns a grade and stage to the cancer that characterize its aggressiveness and the extent to which it has grown or metastasized (spread to other locations in the body). Additional pathology tests determine whether the cancer cells have estrogen receptors (are estrogen positive). CANCER STAGING AND GRADING and estrogen reception provide guidance for CANCER TREATMENT OPTIONS AND DECISIONS.

Treatment Options and Outlook

Total HYSTERECTOMY, a surgical operation to remove the uterus and cervix, is nearly always the first treatment of choice for stage 0, 1, and 2 endometrial cancers. Women who have stage 1 or stage 2 endometrial cancer subsequently undergo adjuvant (follow-up) treatment such as HORMONE THERAPY or RADIATION THERAPY. Very early endometrial cancer (stage 0, also called carcinoma in situ, and stage 1) is nearly always curable.

For stage 3 and 4 endometrial cancer, the first treatment of choice is radiation therapy to shrink the cancer, with follow-up surgery and hormonal therapy (stage 3) or hormonal therapy alone. Surgery may be total hysterectomy with salpingo-oophorectomy (removal of the uterus, cervix, FALLOPIAN TUBES, and OVARIES) or radical hysterectomy (removal of all the organs of reproduction, the fatty layer covering them called the omentum, and nearby LYMPH nodes). Radiation therapy may be external beam (targeted at the pelvis from a machine outside the body) or brachytherapy (implanted radioactive pellets). Though other treatment options are more effective for stage 0, 1, and 2 endometrial cancers, combination CHEMOTHERAPY becomes a treatment option for metastasized endometrial cancer (stage 3 and stage 4).

Most endometrial cancers are hormone sensitive. Hormonal therapy, such as progestins or estrogen antagonists, effectively shrinks cancer tumors in women by depriving their cells of the hormones they need to thrive. Progestin causes endometrial atrophy (shrinkage of the endometrium) and is an option for younger women with stage 0 or stage 1 endometrial cancer who wish to preserve their FERTILITY. Among the estrogen antagonists currently available are aromatase inhibitors and tamoxifen; these therapies require the cessation of ovarian function. Most women who have stage 2 and more advanced endometrial cancer undergo oophorectomy (surgical removal of the ovaries). Aromatase inhibitors block the conversion of TESTOSTERONE to estrogen in adipose (fat) cells throughout the body, the primary means of estrogen production in a woman's body after MENOPAUSE.

Risk Factors and Preventive Measures

Endometrial cancer is most common in women over age 60. Unopposed estrogen therapy (estrogen without progestin, except in women who have had hysterectomies) and long-term tamoxifen use are additional risk factors. OBESITY, INSULIN RESISTANCE, and type 2 DIABETES also increase the risk for endometrial cancer because these conditions result in higher levels of estrogens in the blood circulation. Endometrial cancer follows a predictable path of evolution from endometrial HYPERPLASIA to full-blown cancer, a path that generally takes years or even decades to manifest. This characteristic makes endometrial cancer fairly easy to detect in women who have regular routine medical examinations with pelvic examination.

See also BREAST CANCER; CERVICAL CANCER; HORMONE-DRIVEN CANCERS; METASTASIS; OVARIAN CANCER; PAP TEST; PREVENTIVE HEALTH CARE AND IMMUNIZATION.

endometrial hyperplasia An overgrowth of the endometrium, the tissue that lines the UTERUS. The thickened endometrium fails to slough during MENSTRUATION, thus continuing to accumulate. Often menstruation is minimal or intermittent. Endometrial HYPERPLASIA in which cell DNA remains normal nearly always remains benign (does not become cancerous). Endometrial hyperplasia that consists of both abnormal cells and abnormal cell organization (architecture), though itself benign, is precancerous.

There are four types of endometrial hyperplasia:

- Simple endometrial hyperplasia (also called cystic glandular or mild hyperplasia) is the earliest stage of endometrial hyperplasia. There is excessive growth of the cells of the endometrium in confined locations though the cells and their architecture (structure and arrangement) are normal. The risk for progression to endometrial cancer is minimal; simple endometrial hyperplasia often resolves (goes away) without treatment.
- Complex endometrial hyperplasia features excessive growth of normal cells with irregular architecture, presenting a somewhat higher, though still relatively low, risk for developing into endometrial cancer without treatment. For most women, doctors recommend treatment with progestin, a synthetic form of PROGESTERONE, to halt the actions of estrogen and cause the endometrium to wither and slough. The endometrium generally returns to normal within two or three MENSTRUAL CYCLES.
- Simple endometrial hyperplasia with atypia is a moderate stage of endometrial hyperplasia in which patches of endometrial cells are not only replicating more frequently than normal but have also become abnormal in their DNA (called nuclear atypia). However, the cellular architecture still follows the normal pattern for endometrial tissue. Untreated simple endometrial hyperplasia with atypia progresses to endometrial cancer in about 10 percent of women. Treatment with progestin often resolves the hyperplasia.
- Complex endometrial hyperplasia with atypia is the most serious stage of endometrial hyperplasia. The endometrial cells have abnormal DNA, instructing them to replicate in unstructured and dysfunctional ways. As well, the endometrial tissue that contains the atypical cells is disorganized and erratic. Without treatment, this stage of endometrial hyperplasia progresses to endometrial cancer in a third or more of women. Treatment with progestin usually, though not always, resolves the hyperplasia.

Symptoms and Diagnostic Path

Symptoms of endometrial hyperplasia may include bleeding between menstrual periods, anovulatory periods (menstrual cycles without OVULATION), heavy or prolonged menstrual periods, and PAIN during SEXUAL INTERCOURSE. Some women may experience AMENORRHEA (absence of menstrual periods). Endometrial biopsy, as an independent procedure or after DILATATION AND CURETTAGE (D&C), confirms the diagnosis. Imaging procedures are not usually helpful as they cannot conclusively distinguish between noncancerous and cancerous tumors in the uterus.

Treatment Options and Outlook

In addition to progestin therapy, other treatment options include the surgical operations D&C and HYSTERECTOMY. In D&C the surgeon gently scrapes

away the overgrown endometrium; in hysterectomy the surgeon removes the uterus. In most situations, hysterectomy is appropriate only when complex endometrial hyperplasia with atypia recurs after other treatments or when the risk for endometrial cancer is high for other reasons, though women who are past menopause and have persistent symptoms may opt for hysterectomy to permanently end the hyperplasia.

Risk Factors and Preventive Measures

Any circumstance that increases the presence of estrogen in the BLOOD circulation underlies the development of endometrial hyperplasia. The risk for endometrial hyperplasia is highest in women who have anovulatory periods (menstrual cycles without ovulation), who take unopposed estrogen therapy (estrogen alone), or who take long-term tamoxifen to treat BREAST CANCER. Other factors that increase estrogen within the body are OBESITY, INSULIN RESISTANCE, and type 2 DIABETES. Nutritional EATING HABITS that emphasize foods low in fats, especially saturated fats, and daily physical exercise are the key lifestyle measures that reduce the risk for endometrial hyperplasia.

See also CANCER RISK FACTORS; CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN); CERVIX; DYSPLASIA; DYSFUNCTIONAL UTERINE BLEEDING (DUB); SURGERY BENEFIT AND RISK ASSESSMENT.

endometriosis A condition in which endometrial tissue (the tissue that forms the lining of the UTERUS) grows abnormally in areas outside the uterus. The most common sites are the OVARIES, FALLOPIAN TUBES, peritoneal (abdominal) cavity, gastrointestinal tract (particularly the COLON), and BLADDER, though endometrial tissue may appear in other locations throughout the body. Endometrial growths, also called implants or tumors, respond to the body's changing hormonal environment through the MENSTRUAL CYCLE in the same ways as endometrial tissue within the uterus: They engorge with BLOOD, atrophy, and slough (bleed). Because there is no pathway for bleeding from these distant endometrial implants to leave the body, the blood accumulates in the surrounding tissues. INFLAMMATION develops as part of the IMMUNE RESPONSE, initiating a HEALING process that results in the formation of SCAR tissue.

The growth of endometrial tissue in the fallopian tubes or ovaries blocks the ability of these structures to properly function, a primary consequence of which is impaired FERTILITY. Endometriosis also appears to instigate an abnormal immune response in which phagocytic cells (cells that engulf and consume cellular debris), primarily macrophages, target and kill SPERM and OVA (eggs). About 40 percent of women who seek treatment for INFERTILITY have endometriosis. Endometriosis affects more than five million women in the United States.

Researchers do not know what causes endometriosis or how endometrial tissue arises in sites other than the uterus. Many women who have endometriosis often also have AUTOIMMUNE DISORDERS such as atopic DERMATITIS, ASTHMA, and allergies, giving rise to the suspicion of a dysfunction within the immune system. Some researchers believe endometrial cells escape from the uterus via the fallopian tubes, then migrate through the LYMPH or blood circulation to implant and grow in other locations. Endometriosis tends to progressively worsen over time because the endometrial implants grow under the influence of ESTROGENS, though this growth usually abates with MENOPAUSE. For most women menopause, natural or induced, ends endometriosis.

Symptoms and Diagnostic Path

The primary symptoms of endometriosis are PAIN and infertility. Pain is typically cyclic, following the pattern of the menstrual cycle, and may be moderate to debilitating, especially during MENSTRUATION. Distant endometrial implants also cause pain as they swell and then bleed. The diagnostic path includes comprehensive medical examination with pelvic examination and often pelvic ULTRASOUND. Exploratory laparoscopy provides the definitive diagnosis, allowing the gynecologist to directly visualize the endometrial implants. Diagnostic imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) often can detect distant endometrial implants.

Treatment Options and Outlook

At present there is no cure for endometriosis, though various treatment approaches, medical

and surgical, can control symptoms and improve fertility. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which block the inflammatory response as well as relieve pain, are often adequate to treat mild symptoms in women who wish to become pregnant. HORMONE THERAPY is highly effective to treat moderate to significant symptoms in women who do not desire to become pregnant. Common hormone therapies include

- estrogen and progestin in combination, such as oral contraceptives (birth control pills)
- progestin alone, such as in progestin oral contraceptives or DepoProvera injections
- danazol, an androgen analog (synthetic, weak male HORMONE) that suppresses the menstrual cycle
- GONADOTROPIN-RELEASING HORMONE (GNRH) antagonists such as leuprolide, which shut down the ovaries to prevent them from producing estrogen

Laparoscopic surgery to remove endometrial implants from pelvic structures and the peritoneal cavity may be the only treatment that effectively mitigates symptoms in women who have severe, disabling endometriosis. Therapeutic laparoscopy for endometriosis can provide long-term relief. However, it does not remove distant endometrial implants, which often continue to produce symptoms. As well, endometrial implants will regrow if a few endometrial cells remain.

Risk Factors and Preventive Measures

Factors that increase a woman's risk for endometriosis are unclear. Because endometriosis tends to run in families, researchers believe it may be the result of GENETIC PREDISPOSITION in combination with other, undetermined factors. However, any woman who menstruates can develop endometriosis. There are no measures to prevent endometriosis.

See also ANALGESIC MEDICATIONS; ENDOSCOPY; MACROPHAGE; MONONUCLEAR PHAGOCYTE SYSTEM; PHAGOCYTOSIS; SURGERY BENEFIT AND RISK ASSESSMENT; UTERINE FIBROIDS.

epididymitis INFLAMMATION of the EPIDIDYMIS, nearly always due to INFECTION. The epididymis is a tightly coiled tubule that begins at the base of the testicle and ends at the VAS DEFERENS. The epididymis incubates newly formed SPERM, bringing them to maturation as they migrate through its coils on their journey to the vas deferens. *ESCHERICHIA COLI* INFECTION, CHLAMYDIA, and GONORRHEA are the most common causes of epididymitis—*E. coli* in young boys and men over age 60; chlamydia and gonorrhea in men between ages 25 and 50. Repeated infections may result in permanent INFERTILITY.

Symptoms typically include scrotal PAIN and swelling, discharge from the PENIS, and difficulty urinating. Some men also experience FEVER, NAUSEA, and pain extending into the sides of the abdomen (the flank area). The diagnostic path includes examination to rule out TESTICULAR TORSION and culture of the discharge to identify the responsible PATHOGEN. Treatment is a course of the appropriate ANTIBIOTIC MEDICATIONS when the infection is bacterial. As with all infections, it is essential to complete the entire prescribed course of antibiotics even when symptoms improve. Less commonly, viruses (such as the MUMPS VIRUS) may cause epididymitis. Viral epididymitis resolves without treatment (antibiotic medications cannot treat viral infections).

The doctor may recommend ANALGESIC MEDICATIONS such as acetaminophen or NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen to relieve discomfort and fever; NSAIDs can also relieve inflammation. Ice packs or cold cloths applied to the SCROTUM and supporting the scrotum such as by wearing an athletic supporter may also provide relief.

See also ABSCESS; HEMATOSPERMIA; ORCHITIS; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; URETHRITIS.

episiotomy A surgical incision through the tissues of the PERINEUM to extend the opening of the VAGINA during CHILDBIRTH. The most common types of episiotomy are the midline (median) incision, which extends from the vaginal opening toward the ANUS, and the mediolateral incision, which extends from the vaginal opening diagonally to either side. The obstetrician numbs the tissues of the perineum with an injected local anesthetic (if the woman does not already have epidural anes-

thesia), then makes the incision. After delivery of the baby and the PLACENTA, the obstetrician sutures (stitches) the incision closed.

Though once commonplace as a routine measure to prevent tearing of the vagina and surrounding tissues, episiotomy is now a procedure most obstetricians perform only when it appears that a natural tear will penetrate into the muscles of the perineum or RECTUM. The prevailing belief supporting preventive episiotomy had been that the clean cut of a surgical incision healed more rapidly and with fewer complications than the often jagged wound that occurred with a natural tear (also called a laceration). However, numerous studies have failed to support this premise, and the American College of Obstetricians and Gynecologists (ACOG) now advises against routine episiotomy.

Most episiotomies heal in four to six weeks though some women experience discomfort or PAIN for up to several months, especially with SEXUAL INTERCOURSE. Typically the obstetrician uses sutures the body absorbs as the incision heals. Risks of episiotomy include excessive bleeding, INFECTION, and weakening of the muscles of the pelvic floor that may result in URINARY INCONTINENCE, FECAL INCONTINENCE, and painful sexual intercourse. Many practitioners who provide care for women during PREGNANCY and childbirth advocate prenatal efforts, such as perineal massage to increase tissue elasticity and KEGEL EXERCISES to strengthen and tone the pelvic muscles; perineal massage during labor may also reduce the risk for natural tears and thus lower the likelihood for episiotomy.

See also CESAREAN SECTION; PRENATAL CARE; SURGERY BENEFIT AND RISK ASSESSMENT.

erection The enlarged and hardened PENIS. Erections begin in the male fetus before birth and continue throughout life. An erection is necessary for SEXUAL INTERCOURSE and in an adult man usually occurs as a result of sexual arousal. Erections also occur spontaneously during sleep, usually during rapid eye movement (REM) sleep. A man typically has up to a half dozen nocturnal erections each night. Doctors do not know what causes nocturnal erections though believe they are a consequence of electrical activity in the BRAIN, not of sexual stimulation.

An erection during sexual arousal occurs as a result of interactions between the thoughts and physical stimulation of the penis. The sequence of interactions triggers the release of nitric acid, acetylcholine, EPINEPHRINE, and other neurotransmitters (biochemicals that conduct NERVE impulses). These substances cause the smooth MUSCLE tissue supporting the corpora cavernosa, the two tubelike channels along the top of the penis, to relax. BLOOD flows into the corpora cavernosa. Some of the layers of tissue within the penis contract to help hold the blood within the corpora cavernosa, and valves in the veins that normally carry blood from the penis close. These events cause the size of the penis to increase in length and circumference.

An erection may come to fullness within a few seconds to several minutes, depending on numerous factors such as the man's age and lasts generally until EJACULATION. Some men can sustain an extended erection during sexual activity. Nearly as quickly as the tissues of the penis release nitric acid, they also release the enzyme phosphodiesterase (PDE), which counters the actions of nitric acid and other neurotransmitters to allow blood to flow out of the penis. This action gains momentum after ejaculation or other culmination of sexual activity, serving to reverse the actions of these neurotransmitters. The penis again goes limp (becomes flaccid).

See also CONTRACEPTION; ERECTILE DYSFUNCTION; FERTILITY; MASTURBATION; NEUROTRANSMITTER; PARAPHIMOSIS; PHIMOSIS; PRIAPISM; SEXUAL HEALTH; VEIN.

erectile dysfunction The reduced ability or inability for a man's PENIS to become erect or sustain an erection adequate for SEXUAL INTERCOURSE. Erectile dysfunction, sometimes called impotence, may occur as a physiologic condition, psychologic or emotional condition, or combination. Most commonly, however, all of these factors contribute to the condition. About 25 million men in the United States have chronic (long-term) erectile dysfunction.

Physiologic causes of erectile dysfunction include

- NERVE damage that occurs as a complication of PROSTATECTOMY (surgery to remove the PROSTATE GLAND)

- DIABETES, which progressively damages the body's arteries and nerves
- peripheral NEUROPATHY, which may damage the nerves that supply the penis
- MULTIPLE SCLEROSIS, a degenerative neurologic disorder that causes loss of nerve function in various areas of the body
- ATHEROSCLEROSIS, which may occlude the arteries that serve the penis and slow the flow of BLOOD to the penis
- chronic LIVER disease or chronic kidney disease
- SPINAL CORD INJURY or TRAUMATIC BRAIN INJURY (TBI), either of which may interrupt the flow of nerve impulses between the CENTRAL NERVOUS SYSTEM and the PERIPHERAL NERVOUS SYSTEM

Cigarette smoking is a key contributing factor for neuropathy and atherosclerosis, compounding the effect these conditions have throughout the body. Numerous medications may cause erectile dysfunction as an undesired SIDE EFFECT. The most common culprits are ANTIDEPRESSANT MEDICATIONS, antihypertensive medications to treat HYPERTENSION (high BLOOD PRESSURE), and ANTIHISTAMINE MEDICATIONS to treat seasonal allergies. Fear, stress, anxiety, and DEPRESSION are among the psychologic and emotional causes of erectile dysfunction.

ERECTILE DYSFUNCTION AND HEART DISEASE

Studies suggest erectile dysfunction in otherwise healthy men is a harbinger of HEART disease, notably ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). The small arteries that flood the PENIS with BLOOD during ERECTION appear to show the effects of accumulated arterial plaque earlier than other arteries in the body. Though other arteries of similar size likely occlude to similar extent, men are more likely to notice and pay attention to circumstances that interfere with erection.

Symptoms and Diagnostic Path

The inability to get or sustain an adequate erection is the symptom of erectile dysfunction. The diagnostic path begins with a thorough physical examination, including DIGITAL RECTAL EXAMINATION (DRE) to assess the status of the prostate gland and blood tests to measure the levels of lipids (cholesterol and triglycerides), TESTOSTERONE, GLUCOSE (fasting blood glucose), and liver enzymes. The doctor may desire additional diagnostic procedures, depending on the results of these preliminary tests. Such procedures may include Doppler ULTRASOUND to assess the flow of blood to and within the penis, testing of nerve function and reflexes, and other factors of function. Because a man normally experiences multiple erections during sleep, some tests are done when the man is sleeping (such as the nocturnal penile tumescence test), to measure the characteristics of nocturnal erections.

Treatment Options and Outlook

Treatment targets the underlying cause when it is identifiable. About 85 percent of erectile dysfunction results from physiologic causes. Sometimes treatment is straightforward and relatively easy, such as changing to a different medication when the cause of erectile dysfunction is medication side effect. Often, however, the most effective treatment addresses multiple contributing factors and encompasses medical interventions, lifestyle modifications, and psychologic therapy or counseling.

Medical interventions Phosphodiesterase (PDE) inhibitors, also called selective enzyme inhibitors, are the least intrusive and often most successful medical treatment for erectile dysfunction. The best known of these oral medications to treat erectile dysfunction is sildenafil, first marketed under the trade name Viagra. Other medications in this classification include vardenafil (Levitra) and tadalafil (Cialis). These drugs work by delaying the enzyme-initiated process through which an erection subsides, extending the erection. The erection still requires sexual stimulation to develop; these medications do not cause spontaneous erection. Men who take certain medications to treat HEART disease, such as some antihypertensive medications to treat high blood pressure, cannot take PDE inhibitors because the actions of the drugs are similar and combining them can cause fatally low blood pressure. PDE inhibitors are most effective in men who have mild to moderate vascular disease (such as atherosclerosis) or arterial damage due to diabetes.

Prescription-strength preparations of the herb-derived product YOHIMBE/YOHIMBINE also may extend erections though work through a different

mechanism. Yohimbe (the herb) and yohimbine (the active ingredient derived from the herb) products require a doctor's prescription in the United States because they act on the parasympathetic NERVOUS SYSTEM (a division of the autonomic nervous system that regulates certain involuntary functions). Yohimbe/yohimbine products are most effective in men who have mild to moderate neuropathy (nerve damage). The supplement arginine may also decrease erectile dysfunction by increasing nitric oxide.

Other medications that cause erection are self-injected into the penis or inserted as tiny suppositories (about the size of a grain of rice) into the urethral meatus (opening of the URETHRA at the tip of the penis). These medications contain alprostadil, a formulation of PROSTAGLANDINS, that instigates the sequence of events within the penis that cause it to engorge and stiffen. Unlike oral PDE inhibitors, these medications do cause erection regardless of sexual stimulation because they act directly on the smooth MUSCLE within the penis that causes the corpora cavernosa to relax and fill with blood. The primary drawback to these medications is their form of administration, which limits their appeal as well as the frequency with which a man may use them (no more often than once every five days).

Surgery to repair damaged blood vessels or insert penile implants is an option for erectile dysfunction that does not respond to medications. The most commonly used penile implants are a combination of inflatable tubes, a tiny pump, and small reservoirs that contain a sterile fluid. The man activates the pump, usually placed in the SCROTUM or at the base of the penis, to fill the tubes to acquire an erection. A valve releases the fluid back into the reservoir.

Lifestyle modifications Lifestyle modifications such as weight loss, daily physical exercise, SMOKING CESSATION, and reduced ALCOHOL consumption can improve circulation and nerve function. Exercise in particular also helps reduce stress.

Psychologic therapy Counseling or sex therapy may be helpful when there are emotional factors at play. These factors may cause erectile dysfunction or develop because of it and then perpetuate it. Therapy may be individual or involve the sexual partner.

Risk Factors and Preventive Measures

Erectile dysfunction becomes more common after age 50. The key health risks for erectile dysfunction are cigarette smoking, OBESITY, diabetes, long-term ALCOHOLISM, CARDIOVASCULAR DISEASE (CVD), prostate disease, and kidney disease. Lifestyle significantly influences these factors. Lifestyle measures to reduce these risks include smoking cessation, nutritious EATING HABITS, daily physical exercise, moderation in or cessation of alcohol consumption, and weight management. Medical measures include management of blood lipid levels (cholesterol and triglycerides) and diligent control of blood glucose and INSULIN levels in men who have diabetes through appropriate medication therapy.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; BENIGN PROSTATIC HYPERPLASIA (BPH); DIET AND HEALTH; EXERCISE AND HEALTH; GENERAL ANXIETY DISORDER (GAD); PRIAPISM; PROSTATE HEALTH; SEXUAL HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

F

fallopian tubes A pair of narrow enclosed channels that transport OVA (eggs) from the OVARIES to the UTERUS. The fallopian tubes extend from the top of the uterus, one on each side, curving downward to end just short of the ovaries. The ovary end of the fallopian tube is somewhat fluted with fringelike edges called the fimbriae. The fimbriae float in fluid. At OVULATION the ovary releases an ovum (egg) into the fluid. The fimbriae undulate, drawing the ovum into the fallopian tube. Tiny cilia (hairlike structures) project from the cells that form the tube's inner lining. The cilia move in wavelike motions that pull the ovum along the fallopian tube toward the uterus. If SPERM are present, they may fertilize the ovum on its journey through the fallopian tube. If no sperm are present, the ovum passes into the uterus and out of the body with MENSTRUATION.

A TUBAL LIGATION is a form of permanent CONTRACEPTION (birth control) in which the gynecologist ablates (destroys, such as by electrocautery) or cuts and ties the fallopian tubes to block passage for ova. Rarely, a tubal ligation may spontaneously reconnect. Recurrent infections such as SEXUALLY TRANSMITTED DISEASES (STDS) may affect the fallopian tubes, causing salpingitis or PELVIC INFLAMMATORY DISEASE (PID). Either may result in permanent loss of FERTILITY through scarring that obstructs (blocks) the fallopian tubes.

For further discussion of the fallopian tubes within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also INFERTILITY; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

family planning The process of intentional decision making around having children. Family planning encompasses choices in regard to PREGNANCY, ADOPTION, and not having children. Factors that influence family planning include general health, FERTILITY, personal preferences, religious beliefs, and lifestyle matters such as partnership status and work or career demands. In the United States about half of all pregnancies are intended. One million unintended pregnancies occur in teens. The US government's program of health goals HEALTHY PEOPLE 2010 calls for the availability of appropriate resources (such as education and contraceptive methods) so that all pregnancies are intended.

Planning pregnancy prevention (CONTRACEPTION) and pregnancy (conception) are equally important. More than a half dozen methods of contraception are available, from abstinence and cyclic timing (rhythm method) to sustained-release HORMONE regulation. The choice of contraception should consider availability, ease of use, rate of success, and personal preferences of sexual partners. The most common reason for failure of any given contraceptive method is failing to use it. However, the only certain method for preventing pregnancy is abstinence (not having SEXUAL INTERCOURSE). No other method of birth control is 100 percent certain to prevent pregnancy, though methods such as TUBAL LIGATION and VASECTOMY (operations to produce permanent sterilization) come close.

A key aspect of pregnancy planning is birth spacing—the amount of time between the births of children. From a health perspective, three years or more between births is optimal for both maternal and child health. This spacing allows the mother to fully recuperate between pregnancies as well as to provide the attention that each child needs. Siblings who have three or more years

between them are in different developmental stages for most of their childhood years, requiring different kinds of attention. Providing adequate attention to each child is more difficult when their ages are so close together that their needs are similar. Birth spacing requires either abstinence or some form of contraception between pregnancies to prevent unintended pregnancy.

People may choose adoption (acquiring legal responsibility for a nonbiologic child) as an option for resolving INFERTILITY or because they feel it is a personally desirable or socially responsible approach to creating a family. Other people may choose to have no children, opting instead to define family in other ways.

See also ABORTION; GESTATIONAL SURROGACY.

fertility The ability to conceive a PREGNANCY, and in women to also carry the pregnancy to term. Men and women both become fertile during PUBERTY, when sexual maturity results in the development of SECONDARY SEXUAL CHARACTERISTICS. Men remain fertile all of their lives and are fertile on a continuous basis; women remain fertile through their late 40s or until MENOPAUSE and are fertile on a cyclic, monthly basis.

Female Fertility: Ovulation, Conception, and Pregnancy

Within a narrower context, fertility is the period of time within a woman's MENSTRUAL CYCLE when she is physiologically capable of CONCEPTION. This period of time is the approximately 48 hours before and 24 hours after OVULATION (release of an ovum). The ovum remains receptive to fertilization during the time it travels through the fallopian tube on its way to the UTERUS. SPERM can survive 48 to 72 hours after entering the woman's reproductive tract (such as with SEXUAL INTERCOURSE). A woman can conceive when viable sperm are present in her body when she ovulates.

Knowing the precise timing of ovulation is difficult because it varies somewhat from one menstrual cycle to another. As well, physical illness, trauma, or surgery can affect ovulation and fertility. Several methods may help a woman estimate when she is ovulating. The easiest, though the least precise, is counting 14 days back from the anticipated first day of MENSTRUATION. The days fertility is most likely are 12, 14, and 16 days before the onset of menstruation. This method is imprecise because many women ovulate earlier or later than 14 days and experience variation from one menstrual cycle to another. Other methods may detect when ovulation occurs but cannot predict it before the fact.

The simplest device-oriented measure to estimate a woman's fertile time is basal body temperature. This is the first temperature of the day, taken before getting out of bed and with minimal movement. A woman's body temperature is up to one degree higher after ovulation than before ovulation. The beginning of the rise marks ovulation. Either a regular oral thermometer or a basal body thermometer (which registers only between 96°F and 100°F) works for this purpose. Combining basal body temperature with calendar timing is more accurate than either method alone.

Home ovulation tests may examine saliva or URINE. The urine test, which has been available since the mid-1980s, detects the presence of LUTEINIZING HORMONE (LH) in the urine. The PITUITARY GLAND releases LH to stimulate the luteal, or secretory, phase of the menstrual cycle and the ultimate release of the ovum. The LH test is similar to a home pregnancy test in that the sample of urine causes a change in the indicator when LH is present in the urine. The saliva test, which became available in 2002, allows examination of the saliva for changes in the concentration of potassium chloride. The amount of potassium chloride in the saliva increases during the luteal phase, a reaction to the surge of ESTROGENS that precedes ovulation. The saliva test uses a small microscope, which comes with the test kit, to examine a drop of saliva on a slide for the pattern of potassium chloride. Small spots are normal; fernlike patterns suggest ovulation.

The final element of fertility in women is the ability to sustain pregnancy through birth. Some conceptions are unable to implant, perhaps because of extensive UTERINE FIBROIDS, excessively tipped uterus, malformation of the uterus, and other circumstances in which the uterus cannot support the blastocyst. As many as a third of pregnancies spontaneously abort (miscarry) within the first eight weeks. Spontaneous ABORTION becomes less common after the 14th week.

Though a woman retains fertility for as long as she ovulates and has menstrual cycles (even if irregular), her fertility diminishes as she approaches menopause. Menstrual cycles and ovulation often become irregular in timing, and anovulatory cycles (menstrual cycles without ovulation) become more common. Other factors that influence fertility in women include

- oral contraceptives (birth control pills), which override the body's hormonal regulation of the menstrual cycle, or estrogen suppression therapy, such as to treat severe uterine fibroids or ENDOMETRIOSIS
- TURNER'S SYNDROME
- PREMATURE OVARIAN FAILURE (POF), in which the OVARIES stop functioning before natural menopause
- TUBAL LIGATION (surgery to "tie" or cut the FALLOPIAN TUBES as a permanent form of CONTRACEPTION)
- HYSTERECTOMY (surgery to remove the uterus)
- chronic PELVIC INFLAMMATORY DISEASE (PID), which may SCAR and block the fallopian tubes
- CHEMOTHERAPY or RADIATION THERAPY to treat cancer anywhere in the body

Male Fertility and Conception

Male fertility relies on the motility (movement and thrust), morphology (physiologic form), and volume of sperm present in the ejaculate (SEMEN that leaves the man's PENIS with EJACULATION). Laboratory examination of a sperm sample measures these and other factors; there are no home tests for sperm viability. Sperm can live about 72 hours in the woman's reproductive tract, though the environment of the VAGINA is particularly hostile, and about half of the 500 million or so sperm typically present in a fertile man's ejaculate die during their passage through the it. However, dead and dying sperm are important to fertility because they provide protection and support for living, motile sperm. Dead sperm help form a protective barrier around surviving sperm. The movement of dying sperm helps propel onward the cluster of sperm that remain viable.

One healthy, functioning testicle is adequate to produce enough sperm for fertility. Though a man remains fertile all his life the quality of his sperm (motility, morphology, and other characteristics) tends to decline in his later years (age 70 and older). This may become an issue in regard to fertility if the woman's fertility is marginal. Other factors that influence male fertility include

- inflammatory damage to the TESTICLES due to bacterial or viral INFECTION
- RETROGRADE EJACULATION (semen enters the BLADDER instead of leaving the penis during ejaculation)
- PROSTATECTOMY (surgery to remove the PROSTATE GLAND)
- VASECTOMY (surgery to clip or cut the VAS DEFERENS as a means of permanent contraception) or ORCHIECTOMY (surgery to remove a testicle)
- CRYPTORCHIDISM (undescended testicle), particularly bilateral or delayed diagnosis
- ERECTILE DYSFUNCTION
- chemotherapy or radiation therapy for cancer anywhere in the body

Body temperature also affects male fertility. Normally the SCROTUM (saclike structure that contains the testicles) rises and lowers to maintain ideal temperature for spermatogenesis (production of new sperm). FEVER, sitting in a hot tub, and wearing clothing that holds the scrotum tight against the body are factors that can raise the temperature in the testicles to one at which sperm cannot survive. Though these often are temporary factors, they may be permanent.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; ASSISTED REPRODUCTIVE TECHNOLOGY (ART); STILLBIRTH.

fetus The stage of prebirth development from nine weeks of gestation to birth. The organ systems and major structures take form during the EMBRYO stage, which encompasses the second to the eighth weeks of gestation. During the fetal stage, which is 32 weeks in a full-term PREGNANCY, the systems, organs, and structures grow and develop further sophistication in preparation for independent life. The fetus reaches viability (possibility of surviving on its own) at around 24 weeks of gestation.

HIGHLIGHTS OF FETAL GROWTH

Fetal Age (Gestational Weeks)	Fetal Size	Key Developments
14	3 inches in length	face clearly formed LIVER produces erythrocytes
18	6 inches in length	lanugo (fine HAIR) on head movement may be detectable sucking gastrointestinal tract produces meconium
24	11 inches in length one pound in weight	viability possible with intensive medical care movement apparent eyebrows and eyelashes fingerprints and footprints heartbeat detectable with stethoscope gender detectable with ULTRASOUND startle REFLEX
28	15 inches in length two to three pounds in weight	viability possible eyelids open and close increasing level of BRAIN and NERVOUS SYSTEM functions alveoli in LUNGS
32	17 inches in length four pounds in weight	viability probable body fat BREATHING movements in lungs
36	19 inches in length five to six pounds in weight	viability likely fingernails completely cover fingertips head hair replaces lanugo on head
40	20 to 21 inches in length seven to eight pounds in weight	viable, full term body lanugo disappears lungs mature

See also ABORTION; CHILDBIRTH; CONCEPTION; FETAL ALCOHOL SYNDROME; PRENATAL CARE; STILLBIRTH.

fibroadenoma A benign (noncancerous) tumor of the BREAST composed of a mix of fibrous and glandular tissues. Fibroadenoma is the most common benign breast tumor and most often develops in women under age 30. Researchers do not know what causes fibroadenoma. Many women who develop fibroadenomas have higher than normal levels of ESTROGENS in their BLOOD circulation, though researchers do not know the extent to which this contributes. Fibroadenomas tend to grow during PREGNANCY and shrink after MENOPAUSE, supporting at least some level of hormonal involvement.

Most often the woman detects fibroadenoma as a lump she feels in her breast during BREAST SELF-EXAMINATION (BSE) or the doctor finds the fibroadenoma during the breast exam portion of the

woman's ROUTINE MEDICAL EXAMINATION. Fibroadenomas are characteristically firm, smooth, oval or round, and rubbery in texture. They move freely (are not attached to any surrounding tissues). Biopsy is the only means of definitive diagnosis. MAMMOGRAM is often not helpful in women under age 30 because their breast tissue is quite dense, which makes it difficult to distinguish growths within the breast. As well, the radiologic characteristics of fibroadenoma are very similar to those of breast cysts and BREAST CANCER. ULTRASOUND imaging is sometimes useful to visualize the growth though does not provide definitive diagnosis either.

Some doctors recommend surgery to remove a fibroadenoma because although fibroadenoma does not evolve into cancer, there is a slight possibility cancer may develop within the epithelial cells the fibroadenoma contains. Other doctors suggest a course of watchful waiting when the diagnosis is certain and the fibroadenoma is small. About 10 percent of fibroadenomas spontaneously disappear within a year or two of their discovery. Should the fibroadenoma grow or change, the doctor may biopsy it again or remove it.

See also FIBROCYSTIC BREAST DISEASE.

fibrocystic breast disease A chronic condition in which multiple noncancerous cysts develop in the breasts. As the cysts rupture and heal, they cause clusters of scarlike tissue that form palpable lumps in the BREAST. Though called a disease, this condition is benign (harmless and noncancerous) and very common, affecting more women than not; doctors consider it a normal process associated with the fluctuation of hormones during the MENSTRUAL CYCLE. Fibrocystic breast disease commonly affects both breasts though may affect only one breast.

The health concerns of fibrocystic breast disease are twofold. First, the cysts often cause PAIN and swelling of the breasts, particularly in the week before and the first day or two of the menstrual period. Second, it is not possible to be certain a breast lump is a cyst, raising concerns about BREAST CANCER. As well, though the cysts themselves do not become cancerous, when they are abundant their presence can delay detection of a breast cancer tumor. Fibrocystic breasts are more dense, decreasing the effectiveness of the MAMMOGRAM.

Symptoms and Diagnostic Path

Fibrocystic breasts are typically painful. The discomfort may be persistent, having the quality of dull aching or a sensation of fullness, or cyclic tenderness that intensifies the week before and first few days of the menstrual period. Other symptoms may include

- bumpy or lumpy texture to one quadrant, one side, or all of the breast
- itching or tingling of the nipples
- premenstrual swelling of the breasts

Fibrocystic lumps are characteristically rubbery, smooth, and rounded. With palpation they move within the breast; they are not anchored to the underlying structure of the breast. The diagnostic path includes comprehensive palpation of the breasts. Depending on the woman's age, health history, risk for breast cancer, and other factors, the doctor may use diagnostic imaging procedures such as mammogram and breast ULTRASOUND to obtain additional information about the shape, size, and pattern of the fibrocystic tissue. The doctor may also biopsy several lumps to evaluate their pathology (cell structure and organization) and rule out other causes for the symptoms.

Treatment Options and Outlook

Lifestyle treatments that help mediate discomfort include wearing a supportive bra when symptoms are most significant. Some women get relief by limiting their intake of dietary fats and CAFFEINE, though clinical studies of the correlations between these factors and fibrocystic breasts so far have produced inconclusive and sometimes conflicting findings. Others find that vitamin E, vitamin B_6 (pyridoxine), and the herbal preparation evening primrose oil reduce tenderness and swelling. Medical interventions that may provide relief include NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which reduce INFLAMMATION, and oral contraceptives (birth control pills), which regulate the hormonal cycle. Nearly always the discomforts of

fibrocystic breasts abate with MENOPAUSE and the lumpiness of the breasts diminishes, though some fibrocystic tissue remains.

Risk Factors and Preventive Measures

There are no clear risk factors or measures to prevent fibrocystic breast disease. It is important for women who have fibrocystic breasts to be diligent in performing monthly BREAST SELF-EXAMINATION and to see their health-care providers when they detect any changes in their breasts.

See also BREAST HEALTH; ENDOMETRIOSIS; MEDICINAL HERBS AND BOTANICALS; UTERINE FIBROIDS; VITAMINS AND HEALTH.

G

genitalia The collective term for the organs and structures of reproduction, also called the sex organs or the genitals.

Male genitalia The external male genitalia are the PENIS and SCROTUM; the internal male genitalia are the URETHRA, TESTICLES, VAS DEFERENS, bulbourethral glands (also called Cowper's glands), ejaculatory ducts, seminal vesicles, spermatic cords, and PROSTATE GLAND. All structures of the internal male genitalia occur in pairs except the prostate gland and urethra.

Female genitalia The female external genitalia are the mons pubis, labia majora, labia minora, CLITORIS, Skene's glands, Bartholin's glands, hymen, and vaginal introitus. Collectively the female external genitalia are the VULVA or pudendum. The female internal genitalia are the OVARIES, FALLOPIAN TUBES, UTERUS, CERVIX, and VAGINA.

For further discussion of the genitalia within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also CHILDBIRTH; CONCEPTION; PREGNANCY; SEXUAL HEALTH; SEXUAL INTERCOURSE.

genital trauma Injury to the GENITALIA (organs and structures of reproduction). Genital trauma may occur as the result of accidental injury, ritual genital mutilation, or SEXUAL ASSAULT and may affect the external or internal genitalia. Genital trauma may result in PAIN, structural damage, impaired genitourinary function, SEXUAL DYSFUNCTION, and INFERTILITY.

Male Genital Trauma

Common forms of genital trauma in young boys are in straddle injuries (such as falling onto the bar of a bicycle), blunt force injuries to the groin (such as being struck with a thrown or kicked ball), and toileting injuries (such as the toilet seat falling onto the PENIS or getting the penis or SCROTUM caught in the pants zipper.

In older boys and teens, blunt force injuries are more common. Most organized athletic activities and sports require boys to wear a protective cup to guard against such injuries. In adult men, genital trauma may occur as a result of blunt force and during sexual activity that places unusual or excessive pressure on the erect penis or on the scrotum and TESTICLES.

Some people and organizations that oppose routine male infant CIRCUMCISION (surgical removal of the foreskin) view its practice as a form of male ritualistic genital mutilation.

Female Genital Trauma

Straddle-type injuries are common in young girls, though less frequently from bicycles and more often from activities such as gymnastics and horseback riding. Activities that result in the "splits," whether intentional or accidental, can cause significant bruising and tearing of the external genitals and the PERINEUM (region between the opening of the VAGINA and the ANUS).

Sexual assault is a frequent cause of genital trauma in older girls and women, often resulting from rape (forced, nonconsenting, and violent SEXUAL INTERCOURSE). Health-care providers tend to view most circumstances of female genital trauma with the suspicion that they could represent sexual abuse or assault, in part because it is often the case and in part because the laws in many communities in the United States require them to do so. Hospitals and health-care providers must follow specific procedures to preserve potential evidence when treating sexual assault victims.

Women may experience genital trauma during CHILDBIRTH, particularly with vaginal delivery of a breech presentation (baby born bottom first) or a large baby. Some women have birth-related traumatic tearing of the perineum, and others have episiotomy in an attempt to limit the extent of trauma or enlarge the vaginal opening to allow the baby to pass. The resulting injuries may require surgical repair and sometimes result in long-term complications affecting urinary continence, fecal continence, and pleasure during sexual intercourse.

Female ritual genital mutilation, also called female circumcision, remains common in some cultures despite widespread opposition from the World Health Organization (WHO), Amnesty International, and other health and human rights organizations worldwide. Within such cultures ritual genital mutilation may be a rite of passage, a mark of ownership, or a religious practice conducted in early childhood by nonmedical practitioners, without ANESTHESIA and often under unsanitary conditions. Complications are common and often severe. WHO and other organizations have made it a goal to eliminate ritual genital mutilation worldwide.

See also PRIAPISM; TESTICULAR TORSION; VULVODYNIA.

gestational diabetes The development of INSULIN RESISTANCE or type 2 DIABETES during PREGNANCY. Gestational diabetes develops between 24 and 28 weeks of pregnancy. Doctors believe the rising levels of hormones the PLACENTA produces at this point in pregnancy interfere with the ability of the woman's body to properly metabolize INSULIN. Insulin production remains normal. Diabetes that manifests earlier than 24 weeks in pregnancy is nearly always diabetes that was undetected at the start of the pregnancy. Gestational diabetes goes away shortly after delivery, though women who have gestational diabetes have increased risk for developing type 2 diabetes later in life.

Untreated gestational diabetes poses a health risk primarily for the FETUS. The excessive GLUCOSE (sugar) that circulates in the mother's BLOOD crosses the placenta. When it reaches the fetus the excessive glucose fuels fetal growth, resulting in fetal size up to 20 percent greater than normal. This growth becomes problematic within the UTERUS as the fetus cannot move as freely. Adequate prenatal movement is important for proper muscular development. A fetus larger than about eight pounds often has difficulty passing through the birth canal. The circumstance of an overly large fetus, called macrosomia, often necessitates birth by CESAREAN SECTION (surgical delivery) to safeguard the health of both baby and mother. As well, the newborn infant may experience HYPOGLYCEMIA (low blood glucose) in the first hours after birth.

Symptoms and Diagnostic Path

Most often gestational diabetes has few noticeable symptoms. When symptoms do occur they may include frequent URINATION, increased thirst, and increased hunger. Because these are common in pregnancy, however, they are difficult to distinguish as symptoms of diabetes. Routine URINE tests at each prenatal doctor visit screen for the overflow of glucose in the urine, which indicates high blood glucose. Health-care providers routinely test for elevated glucose in the woman's blood circulation between the 24th and 28th weeks of pregnancy. The most common such test is the three-hour glucose tolerance test. Findings of an elevated blood glucose level at two or more of the four drawings of blood over the course of the test generally establishes the diagnosis of gestational diabetes.

Treatment Options and Outlook

Many women are able to manage gestational diabetes through nutritional EATING HABITS and daily exercise. Women for whom lifestyle measures do not maintain stable blood glucose levels typically require insulin injections through the remainder of pregnancy. The safety of oral antidiabetes medications in pregnancy remains undetermined, though some doctors offer this treatment. Diligent management of blood glucose levels helps maintain normal growth and weight of the fetus.

In nearly all women gestational diabetes goes away within a week of delivery and for a third of women diabetes is never again a health concern. However, in some women who have high risk for diabetes in the first place gestational diabetes may persist to become conventional diabetes. One in

five women who has gestational diabetes will develop conventional diabetes within five years of her baby's birth, and about two thirds of women will develop the condition later in life.

Risk Factors and Preventive Measures

Any pregnant woman can develop gestational diabetes. Factors that increase the risk for gestational diabetes include

- gestational diabetes in a previous pregnancy
- obesity
- African American or Hispanic heritage
- age 25 or older

Because gestational diabetes results from the effects in the woman's body of hormones the placenta produces, there are no certain measures to prevent its development. Lifestyle measures to maintain nutritious eating habits, daily exercise, and healthy weight help the body use glucose and insulin as efficiently as possible.

See also ECLAMPSIA; LIFESTYLE AND HEALTH; PREECLAMPSIA; WEIGHT LOSS AND WEIGHT MANAGEMENT.

gestational hypertension See PREECLAMPSIA.

gestational surrogacy A circumstance in which one woman carries a PREGNANCY for another woman who cannot carry it herself. Gestational surrogacy is among the possible solutions for INFERTILITY, typically in circumstances such as uterine malformation that prevent successful implantation or carrying the pregnancy to term.

The woman who carries the pregnancy is the gestational surrogate or gestational carrier; the woman to whom the pregnancy belongs is the intended parent. The gestational surrogate may be a relative of or a woman or couple desiring the pregnancy, may know the woman or couple desiring the pregnancy, or may make herself available to a FERTILITY clinic for the purpose of gestational surrogacy. The pregnancy takes place through some form of ASSISTED REPRODUCTIVE TECHNOLOGY (ART), typically in vitro fertilization. ART may use the intended mother's egg, a donor egg, or the gestational surrogate's egg fertilized with the intended father's SPERM or donor sperm. As with any pregnancy, multiple factors affect the success of these efforts.

Gestational surrogacy entails intense emotional and legal complexities as well as physical and health risks for the gestational surrogate. Women considering gestational surrogacy, whether as intended parent or gestational surrogate, should obtain legal advice before initiating the process. It is crucial for all participants to fully understand the risks and to agree, via written contract, to the conditions of the arrangements. In the United States each state determines the legal status of surrogacy; many states restrict financial arrangements with and payments to gestational surrogates as well as tightly regulate the myriad aspects of legal parentage and responsibility. Though gestational surrogacy is often a positive experience for all involved, the potential for complications and problems exists.

See also ADOPTION; FAMILY PLANNING.

gynecomastia BREAST enlargement in a man. Gynecomastia may be a symptom of OBESITY or hormonal imbalance such as may occur during PUBERTY or with various endocrine disorders that affect the production of TESTOSTERONE. Advanced CIRRHOSIS, LIVER CANCER, and chronic ALCOHOLISM often produce gynecomastia because the resulting dysfunction of the LIVER alters how the adipose (fat) cells metabolize ESTROGENS. Estrogen levels in the BLOOD circulation tend to rise with chronic liver disease or damage to the liver. Gynecomastia is also a characteristic SIDE EFFECT of HORMONE THERAPY to treat PROSTATE CANCER, again because the balance of estrogen in the blood circulation increases. Treatment for gynecomastia depends on the underlying cause.

See also MASTALGIA.

H

hematospermia BLOOD in the SEMEN that may be apparent with EJACULATION. Trauma and INFECTION are the main causes of hematospermia. SEXUALLY TRANSMITTED DISEASES (STDS), notably GONORRHEA and CHLAMYDIA, are common infections that irritate and inflame the URETHRA, often causing bleeding into both the URINE (HEMATURIA) and the semen as either passes through the urethra to leave the body. Less common causes of hematospermia include bleeding disorders (health conditions or medication induced); severe HYPERTENSION (high BLOOD PRESSURE); and, in men over age 50, PROSTATE CANCER. Diagnostic and therapeutic efforts focus on identifying and treating the underlying cause.

See also EPISTAXIS; URETHRITIS.

hot flashes Sudden episodes of flushing and sweating that occur with the fluctuating HORMONE levels that precede MENOPAUSE or as a consequence of HORMONE THERAPY such as to treat HORMONE-DRIVEN CANCERS. Though researchers do not know the precise mechanisms of hot flashes, they believe the sudden drops in ESTROGENS affect the thermoregulatory centers in the BRAIN that cause the body to function as though it must reduce body temperature. SKIN flushing and sweating are among the methods the body uses to accomplish such reduction. Hot flashes associated with menopause improve and usually go away when the body's estrogen levels stabilize.

Lifestyle measures to mitigate the discomfort of hot flashes include dressing in layers to allow rapid cooling, drinking cool fluids at the onset of a hot flash, minimizing CAFFEINE consumption, and avoiding foods that are high in tyramines, including red wine, aged cheese, smoked meats, and concentrated yeasts such as miso. Medical treatments for hot flashes include selective serotonin reuptake inhibitor (SSRI) medications, a classification of antidepressant medication that appears to reduce the frequency and intensity of hot flashes, or short-term hormone replacement therapy (HRT). Alternative and complementary approaches to relieve hot flashes include ACUPUNCTURE and botanical remedies such as BLACK COHOSH and SOY.

See also ANTIDEPRESSANT MEDICATIONS; MEDICINAL HERBS AND BOTANICALS; PREMATURE OVARIAN FAILURE (POF).

hydrocele A fluid-filled growth, similar to a cyst, that develops in the SCROTUM. Most hydroceles are congenital (present at birth) and occur as a result of incomplete closure of the channel through which the testicle descends from the abdomen to the scrotum. The defect allows peritoneal fluid to seep from the abdominal cavity into the scrotum. A congenital hydrocele, also called a primary hydrocele, appears as a variable and usually painless enlargement of the scrotum. The size of the enlargement may fluctuate with changes in abdominal pressure, increasing with activities such as bearing down (Valsalva maneuver), coughing, sneezing, or, in infants, vigorous crying. Secondary hydrocele may develop after viral INFECTION (more common in children) or trauma to the scrotum.

The preliminary diagnosis of hydrocele is clinical, based on the scrotum's transluminency. In this simple test the doctor holds a bright, focused penlight against the side of the scrotum. When the cause of scrotal swelling is hydrocele, the light passes uniformly through the tissues of the scrotum. Most other causes of scrotal swelling are not transluminent. An OPERATION to repair a primary hydrocele is the treatment of choice; surgical

examination of the swelling subsequently confirms the diagnosis. The operation closes the defect that allows fluid to seep into the scrotum. Complications after surgery are rare though could include anesthetic reaction, unusual bleeding, or infection. Secondary hydrocele generally heals on its own.

See also HERNIA; TESTICLES; VIRUS.

hypogonadism Dysfunction of the gonads resulting in inadequate production of sex hormones. In men the TESTICLES (also called testes) are the gonads that produce ANDROGENS and in women the OVARIES are the gonads that produce ESTROGENS. In primary hypogonadism the ovaries or testicles themselves fail. Genetic reasons for such failure are TURNER'S SYNDROME in females and KLINEFELTER'S SYNDROME in males. These genetic disorders result from errors in the sex chromosomes.

Hypogonadism may also be central, a result of problems with the endocrine mechanisms that regulate the function of the ovaries or testicles. The most common of such problems are traumatic injury, surgery, RADIATION THERAPY, and CHEMOTHERAPY. Tumors of the PITUITARY GLAND, untreated HYPOTHYROIDISM, and EATING DISORDERS such as anorexia nervosa that result in severe NUTRITIONAL DEFICIENCY, may also cause central hypogonadism.

Symptoms of hypogonadism depend on the developmental stage of the individual. Primary hypogonadism that occurs in childhood, such as resulting from Turner's syndrome or Klinefelter's syndrome, causes absence of PUBERTY and failure to develop SECONDARY SEXUAL CHARACTERISTICS. Hypogonadism that develops in adulthood results in menopausal symptoms such as HOT FLASHES in women and diminished LIBIDO, ERECTILE DYSFUNCTION, and sparsity of facial HAIR in men.

The diagnostic path includes BLOOD tests to measure blood levels of estrogen, TESTOSTERONE, FOLLICLE-STIMULATING HORMONE (FSH), LUTEINIZING HORMONE (LH), and thyroid hormones. Treatment for primary hypogonadism in most situations is HORMONE THERAPY to restore blood levels of the sex hormones to normal levels for the person's age. When hypogonadism is central, treatment targets the underlying cause. Hormone therapy initiates puberty when hypogonadism occurs in childhood. However, FERTILITY issues may remain even with treatment though other symptoms typically improve.

See also CHROMOSOMAL DISORDERS; CHROMOSOME; GYNECOMASTIA; HORMONE; SEX CHROMOSOME; THYROID GLAND.

hysterectomy A surgical OPERATION to remove the UTERUS. Hysterectomy may be treatment for ENDOMETRIAL CANCER or for noncancerous conditions that cause significant symptoms and do not respond to less invasive treatments. Among such conditions are UTERINE FIBROIDS, UTERINE PROLAPSE, DYSFUNCTIONAL UTERINE BLEEDING (DUB), and ENDOMETRIOSIS. Whatever its reason, a consequence of hysterectomy is immediate loss of FERTILITY. Hysterectomy is the second-most common operation women undergo in the United States; CESAREAN SECTION (surgical CHILDBIRTH) is the most common. Surgeons in the United States perform more than 600,000 hysterectomies each year.

Surgical Procedure

The ANESTHESIA for hysterectomy may be regional, such as epidural block, with sedation or general (deep sleep). The choice of anesthesia depends on the type of hysterectomy the woman is having, the woman's preferences, and the recommendations of the surgeon and anesthesiologist.

A simple hysterectomy removes only the uterus (sometimes called a supracervical hysterectomy); a total hysterectomy removes the uterus and CERVIX. Both operations leave the OVARIES in place to continue providing hormones that carry the woman to a natural MENOPAUSE if she has not already reached that stage of her life. Radical hysterectomy may be necessary when endometrial cancer or CERVICAL CANCER is the reason for the operation. In radical hysterectomy the surgeon removes the uterus, cervix, and upper VAGINA along with much of the tissue that supports these structures.

The operation may be an OPEN SURGERY, in which the surgeon makes a long incision through the SKIN and layers of MUSCLE to expose the uterus, or laparoscopically assisted vaginal hysterectomy, in which the surgeon removes the uterus through multiple small incisions in the abdomen and vagina and removes the uterus with the aid of a lighted, magnifying laparoscope that displays the pelvic structures on a monitor. A laparoscopically

assisted vaginal hysterectomy is somewhat more complex for the surgeon to perform though significantly faster recovery for the woman. It is an appropriate option when hysterectomy is to treat noncancerous conditions.

A laparoscopically assisted vaginal hysterectomy generally requires no more than an overnight stay in the hospital the night after the surgery. A woman often can return to regular activities in about six weeks with the laparoscopic operation. The typical hospital stay for open hysterectomy is three to five days, with full recovery and recuperation in about eight weeks.

Risks and Complications

The primary risks associated with hysterectomy are possible excessive bleeding, BLOOD clots, and INFECTION. Complications may include damage to the nerves that control the bowel or BLADDER that results in FECAL INCONTINENCE or URINARY INCONTINENCE or damage to the structure of the bladder or ureters (tubelike structures that drain URINE from the KIDNEYS to the bladder). These complications are uncommon though may have long-term consequences. When the surgeon leaves the FALLOPIAN TUBES and ovaries intact, these structures sometimes atrophy (shrink). Women who have total hysterectomies with removal of the cervix sometimes experience PAIN during SEXUAL INTERCOURSE for the first few months after surgery. Women who have hysterectomies tend to enter menopause somewhat earlier even when they retain their ovaries.

Outlook and Lifestyle Modifications

Most women return to full, regular activities within two months of surgery (and many sooner). Hysterectomy means the end of MENSTRUATION (though not necessarily the start of menopause), which is sometimes an emotional adjustment. The relief of symptoms related to the condition that necessitated the hysterectomy is sometimes profound, allowing the woman to return to a lifestyle and activities that she had long enjoyed but had stopped participating in because of the symptoms. In circumstances other than cancer, it is important for a woman to understand the nonsurgical options that are available to treat her condition so she can make a fully informed decision.

See also CANCER TREATMENT OPTIONS AND DECISIONS; OOPHORECTOMY; SEXUAL HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT.

hysteroscopy A diagnostic or therapeutic procedure to examine the interior of the UTERUS using a lighted magnifying endoscope. Hysteroscopy is an outpatient surgical procedure that requires regional or general ANESTHESIA. After the administration of anesthesia the gynecologist dilates the CERVIX and inserts the lighted, flexible tube of the hysteroscope into the uterus and fills the uterus with carbon dioxide gas or sometimes liquid saline solution to push the uterine walls apart.

The hysteroscope allows the gynecologist to closely examine the entire endometrium (lining of the uterus) and the entries to the FALLOPIAN TUBES. The gynecologist may use the hysteroscope to obtain tissue samples for biopsy, remove UTERINE FIBROIDS or polyps, and repair minor injuries to the wall of the uterus and certain congenital malformations such as uterine septum.

The risks of hysteroscope include those of anesthesia as well as INFECTION, excessive bleeding, and uterine perforation (puncture of the uterine wall). These risks are uncommon though may require further treatment. Infection requires treatment with ANTIBIOTIC MEDICATIONS. Uterine perforation usually heals on its own. Excessive bleeding may require medications or follow-up surgery to control. Minor bleeding and discomfort (cramping) are normal after hysteroscopy and may continue for a few days.

See also COLPOSCOPY; ENDOSCOPY; SURGERY BENEFIT AND RISK ASSESSMENT.

I

infertility The inability to conceive or maintain a PREGNANCY. Infertility may be transitory (relate to a specific set of circumstances), treatable, or permanent. Infertility affects about 10 percent of Americans who attempt pregnancy.

There are numerous possible causes of infertility that can affect any of the various stages in the process of CONCEPTION. Causes may affect the woman, the man, or the couple in equal distribution. One of the most significant is the woman's age. An increasing number of women in the United States delay starting their families until completing their education and establishing their careers, the average age of first pregnancy is age 30. Though a woman can remain fertile into her late 40s, the likelihood of conception appreciably diminishes each year after age 35.

Infertility is highly emotional for most people. Infertility often comes as a shock, particularly for younger people who had no reason to suspect they were not fertile. Some people feel guilt or regret about choices made earlier in life in regard to CONTRACEPTION and FAMILY PLANNING. Diagnostic procedures and treatment approaches can be invasive and expensive and are without assurances. Though ASSISTED REPRODUCTIVE TECHNOLOGY (ART) is highly advanced and makes pregnancy possible for thousands of couples every year, it nonetheless is unable to help two thirds of couples who cannot conceive.

Female factor infertility In female factor infertility the reason for infertility rests with the woman. A third of infertility circumstances arise from female factors. Ovulatory dysfunction is the most common of them and may result from age, genetics, health conditions, or medical treatments. Blocked FALLOPIAN TUBES are also common. Previous ECTOPIC PREGNANCY, abdominal or pelvic surgery, and complications from untreated SEXUALLY TRANSMITTED DISEASES (STDS) may SCAR and otherwise damage the fallopian tubes. Congenital anomalies of the reproductive organs, such as malformations of the UTERUS, may prevent implantation. EATING DISORDERS such as anorexia nervosa and OBESITY influence the body's endocrine functions and OVULATION. Cigarette smoking, excessive ALCOHOL consumption, and substance abuse also affect FERTILITY.

FEMALE INFERTILITY FACTORS

age over 35	excessive ALCOHOL use
anorexia nervosa	CHEMOTHERAPY
cigarette smoking	CUSHING'S SYNDROME
DIABETES	ENDOMETRIOSIS
OBESITY	OVARIAN CYST
PELVIC INFLAMMATORY DISEASE (PID)	PITUITARY GLAND dysfunction
PREMATURE OVARIAN FAILURE (POF)	POLYCYSTIC OVARY SYNDROME (PCOS)
RADIATION THERAPY	previous ECTOPIC PREGNANCY
substance abuse	SICKLE CELL DISEASE
untreated HYPOTHYROIDISM	TURNER'S SYNDROME
uterine malformations	UTERINE FIBROIDS

Male factor infertility In male factor infertility the reason for infertility rests with the man. A third of infertility circumstances arise from male factors. Male infertility factors may result from problems with spermatogenesis (production of SPERM), SEMEN production, ERECTION and EJACULATION, sperm count, sperm morphology (structure), and sperm motility (movement). Body temperature and scrotal temperature are crucial for spermatogenesis and sperm survival. Circumstances that prevent the SCROTUM from dropping, such as tight clothing, or sustained exposure to heat, such

as sauna or hot tub use, may affect sperm viability. Such effects may be temporary or permanent. Viral infections such as the MUMPS and bacterial EPIDIDYMITIS may damage or destroy testicular tissue. CHROMOSOMAL DISORDERS such as KLINEFELTER'S SYNDROME and endocrine disorders may affect TESTOSTERONE production. Congenital absence of the VAS DEFERENS, which often occurs in men who have CYSTIC FIBROSIS, prevents sperm from leaving the TESTICLES.

MALE INFERTILITY FACTORS

agricultural pesticide exposure	ATHEROSCLEROSIS
CHEMOTHERAPY	chronic ORCHITIS
chronic PROSTATITIS	chronic URETHRITIS
cigarette smoking	CRYPTORCHIDISM
CUSHING'S SYNDROME	CYSTIC FIBROSIS
DIABETES	DOWN SYNDROME
ERECTILE DYSFUNCTION	excessive ALCOHOL consumption
HYDROCELE	KLINEFELTER'S SYNDROME
HYPOGONADISM	low SPERM count
low SEMEN volume	malformed sperm
low sperm motility	prolonged elevated body temperature
OBESITY	SICKLE CELL DISEASE
RADIATION THERAPY	substance abuse
RETROGRADE EJACULATION	testicular trauma
SPERMATOCELE	untreated HYPOSPADIAS
TESTICULAR CANCER	viral or bacterial EPIDIDYMITIS
untreated EPISPADIAS	
VARICOCELE	

Combined factor infertility In combined factor infertility the reason for infertility results from the unique combination of factors each partner brings to the couple. A third of infertility circumstances arise from combined factors or remain unknown in their origin. Combined factors may be elements that, on their own, would not be sufficient to prevent conception. In particular combinations, however, these elements result in infertility. The woman's IMMUNE SYSTEM may generate antibodies that attack the man's sperm. Combined factor infertility is often the most difficult to sort out and treat.

Symptoms and Diagnostic Path

The primary symptom of infertility is the absence of pregnancy after one year of unprotected SEXUAL INTERCOURSE when pregnancy is the desired outcome. The diagnostic path begins with comprehensive medical examination, including PELVIC EXAMINATION for women, and detailed history of attempts to conceive. Further diagnostic procedures depend on the preliminary findings and suspicions, though typically include laboratory tests for STDs, BLOOD tests for antibodies and HORMONE levels for the woman, and semen analysis for the man.

Additional diagnostic procedures for the woman may include

- basal body temperature journaling over several months to assess ovulation
- pelvic or transvaginal ULTRASOUND to examine the OVARIES and reproductive organs
- analysis of vaginal fluids to assess acidity (pH) and mucus
- hysterosalpingogram, a contrast medium X-RAY examination of the uterus and fallopian tubes
- karyotyping to detect chromosomal abnormalities such as TURNER'S SYNDROME
- exploratory laparoscopy to visually examine the internal pelvic structures

Additional diagnostic procedures for the man may include

- blood tests to measure hormone levels
- scrotal ultrasound to detect HYDROCELE, VARICOCELE, or SPERMATOCELE
- karyotyping to detect chromosomal abnormalities such as Klinefelter's syndrome

Treatment Options and Outlook

Treatment targets the identified or suspected cause. Basic approaches include frequent sexual intercourse, sexual positions that support conception, and timing sexual intercourse with ovulation. These basic measures result in conception within two years in about a third of couples. Other straightforward solutions may include treatment for infections or endocrine disorders (such as previously undiagnosed HYPOTHYROIDISM or ADRENAL INSUFFICIENCY).

Further treatment is more invasive. In men, such treatment may consist of surgery to repair hydrocele, varicocele, or spermatocele. Testosterone supplementation often improves sperm

production and erectile function in men whose blood testosterone levels are low. In women, further treatment may include surgery to correct or repair various situations that contribute to or cause female factor infertility such as abdominal adhesions, ENDOMETRIOSIS, UTERINE FIBROIDS, certain uterine malformations, blocked fallopian tubes, and OVARIAN CYST. Hormone supplementation may regulate the MENSTRUAL CYCLE to encourage or stimulate ovulation ("superovulation") in women. Some hormones used in this way are off-label (not approved for infertility treatment though approved for other uses) in the United States.

Fertility experts select hormone therapies according to the underlying cause for ovulatory dysfunction, the woman's age, and any existing health conditions. Hormone treatment for infertility may have serious side effects, risks, and complications, including HOT FLASHES, mood swings, ovarian cyst formation, increased risk for spontaneous ABORTION early in pregnancy (miscarriage), and high risk for pregnancy with multiples (twins or greater). The long-term risks associated with fertility drugs, for the women who take them as well as the children conceived with their assistance, remain uncertain because the drugs have not been in use long enough to allow comprehensive studies.

MEDICATIONS USED TO STIMULATE OVULATION

bromocriptine
cabergoline
clomiphene citrate
FOLLICLE-STIMULATING HORMONE (FSH)
GONADOTROPIN-RELEASING HORMONE (GNRH) analogs
human chorionic gonadotropin (hCG)
human menopausal gonadotropin (hMG)
letrozole
metformin

ART methods to combine sperm and OVA may be appropriate when there are no measures to correct the cause of infertility or attempted treatments have not succeeded.

Risk Factors and Preventive Measures

The primary risk factor for infertility is age. Though the time frame of fertility is clearly defined in women, fertility diminishes to some degree in men as they grow older. Lifestyle risk factors include cigarette smoking, alcohol consumption, environmental hazard exposure (such as pesticides), and obesity. Lifestyle also influences some health risks for infertility such as DIABETES, ATHEROSCLEROSIS, and infection with STDs. Risks for which there are no preventive measures include GENETIC DISORDERS and chromosomal disorders, CONGENITAL ANOMALY of the reproductive organs, POLYCYSTIC OVARY SYNDROME (PCOS), PREMATURE OVARIAN FAILURE (POF), endocrine disorders, and AUTOIMMUNE DISORDERS.

See also ADOPTION; AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; AMENORRHEA; BIRTH DEFECTS; FETAL ALCOHOL SYNDROME; GENITAL TRAUMA; KARYOTYPE; OFF-LABEL USE; PUBERTY; SMOKING AND HEALTH; SMOKING CESSATION; SURGERY BENEFIT AND RISK ASSESSMENT; TUBAL LIGATION; VASECTOMY.

intraductal papilloma A benign (noncancerous) tumor that grows within a lactiferous duct (milk duct) of a woman's BREAST. Intraductal papilloma is the most common cause of nipple discharge, which is its primary symptom. The discharge may be milky, clear, or blood tinged. A woman may notice only slight staining on her clothing. There is usually no PAIN or discomfort associated with intraductal papilloma.

The tumor causing symptoms may be too small for the woman or her health-care provider to feel, though may appear on MAMMOGRAM and usually shows up on ULTRASOUND of the breast. Other diagnostic procedures may include a contrast X-RAY called a ductogram and laboratory analysis of the nipple discharge. Biopsy of the papilloma, usually in combination with its surgical removal, provides definitive diagnosis. Intraductal papilloma occasionally recurs.

See also BREAST CANCER; BREAST HEALTH; FIBROCYSTIC BREAST DISEASE.

K–L

Klinefelter's syndrome A chromosomal disorder affecting only males in which there is at least one extra X CHROMOSOME. The normal chromosomal configuration for a male is XY; the female configuration is XX. The extra X chromosome in a male, which doctors commonly designate as 47 XXY, dilutes the SECONDARY SEXUAL CHARACTERISTICS. Men who have Klinefelter's syndrome often do not produce SPERM and thus are infertile (unable to cause PREGNANCY).

Klinefelter's syndrome often does not become apparent until a boy enters (or fails to enter) PUBERTY. Secondary sexual characteristics are slow to develop and may appear effeminate, with small GENITALIA, enlarged breasts (GYNECOMASTIA), and little facial HAIR. LEARNING DISORDERS are also common in boys who have Klinefelter's syndrome, though researchers are uncertain of the reason for this. Adult men often experience SEXUAL DYSFUNCTION such as low LIBIDO, ERECTILE DYSFUNCTION, and INFERTILITY.

The diagnostic path includes BLOOD tests to measure the levels of TESTOSTERONE, LUTEINIZING HORMONE (LH), and FOLLICLE-STIMULATING HORMONE (FSH). Karyotyping, a representation of the chromosomal configuration of the cells, shows the extra X chromosome (and in some men, more than one extra X chromosome). Treatment is TESTOSTERONE supplementation to restore to normal the level of testosterone in the blood circulation. Testosterone supplementation generally results in increased masculinization (appearance of secondary sexual characteristics) such as thickened beard growth, deepened voice, enlarged PENIS and TESTICLES, and increased MUSCLE mass and definition. Treatment is generally lifelong.

See also CHROMOSOMAL DISORDERS; GENETIC DISORDERS; KARYOTYPE; TURNER'S SYNDROME.

letdown reflex The release of milk from the lactiferous glands and ducts to the nipple of the BREAST to initiate BREASTFEEDING (nursing). The first sucking motions the infant makes when attaching to the nipple are rapid and pulling. These motions stimulate the release of OXYTOCIN from the PITUITARY GLAND, which causes the tissues around the ducts to contract to push the milk to the nipple. The mother feels this release and the initial flow of milk as a tingling sensation. The more full of milk the breasts are the more intense the sensation. Letdown occurs multiple times during a breastfeeding session. Other events may also stimulate the letdown REFLEX, such as the sound of the infant's cry. Letdown affects both breasts, often causing milk to leak from the un-nursed breast.

See also PREGNANCY.

libido The level of sexual desire an individual feels, also called sex drive. Libido represents a complex interaction between the mind and the sex hormones. Low hormonal levels often result in reduced libido. In men the HORMONE associated with libido is TESTOSTERONE; in women both ESTROGENS and testosterone play roles in libido. Numerous medications, serious or chronic illness, long-term ALCOHOLISM, and substance abuse may also reduce libido. As well, libido typically slows with age.

Indications or symptoms of low libido may include

- lack of interest in sex
- lack of sexual arousal
- inability to reach ORGASM
- ERECTILE DYSFUNCTION in men
- reduced vaginal lubrication in women

Hormone supplementation often improves libido when hormone levels are the cause for its decline. Treating health conditions that may cause low libido, or changing medications that can affect libido, is sometimes all the treatment that is necessary. Libido also often has significant emotional and psychologic components. Treatment for low libido depends on its identifiable causes.

See also SEXUAL DYSFUNCTION; SEXUAL HEALTH; SEXUAL INTERCOURSE.

M–N

mammogram An X-RAY examination of the BREAST. The most common use of mammogram is for early detection of BREAST CANCER. However, mammogram may be a diagnostic tool in the evaluation of various conditions that affect the breasts. Most abnormal findings mammograms detect are not cancer.

Most often a woman stands for a mammogram. The technologist places one breast on a shelf on the X-ray machine, beneath which is the X-ray film. A moving shelf then compresses the breast against the shelf to somewhat flatten the breast tissue for better visualization. With routine screening mammogram the technologist takes two X-rays of each breast, one from the side and one from above. The entire procedure—positioning and taking the images—takes about 10 minutes. With diagnostic mammogram the technologist takes up to five images, in different positions, of each breast. The entire procedure for diagnostic mammogram takes about 15 minutes.

Though mammogram is generally quick and painless, some women experience discomfort with the compression of their breasts. Women who are still menstruating should have routine mammograms two weeks after the end of their menstrual periods to minimize discomfort, as the breasts are least sensitive at this time.

Most health-care providers recommend routine screening mammograms beginning at age 40 for women who have no unusual risks for breast cancer—every two years between ages 40 and 50 and once a year after age 50. Women who have had breast cancer or have three or more risk factors for breast cancer should talk with their doctors about the appropriate intervals for mammogram. Because the breast tissue of menstruating women is very dense it blocks visualization of abnormalities, making screening mammogram impractical in younger women. With MENOPAUSE the breast tissue becomes considerably less fatty and dense, so abnormal growths are readily obvious. Mammogram often can detect growths and tumors in the breast before they reach a size at which the woman or her health-care provider can feel them.

See also BREAST SELF-EXAMINATION; CANCER PREVENTION; FIBROCYSTIC BREAST DISEASE; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

mastalgia Painful breasts. Cyclic mastalgia in women occurs commonly with MENSTRUATION. Noncyclic mastalgia in women may indicate MASTITIS (INFLAMMATION, often the result of bacterial INFECTION). Mastalgia in women is also common during PREGNANCY and BREASTFEEDING. Mastalgia is uncommon in men and signals an underlying condition that requires a doctor's evaluation.

Mastalgia is a symptom rather than itself a health condition. The diagnostic path attempts to pinpoint the cause of the PAIN. Diagnostic procedures the doctor may conduct include breast ULTRASOUND and MAMMOGRAM (X-RAY of the BREAST). Treatment targets the underlying cause.

See also GYNECOMASTIA.

mastectomy A surgical OPERATION to remove the BREAST. Mastectomy is most commonly a treatment for BREAST CANCER. Women who have extraordinarily high risk for breast cancer (such as because of family history or known MUTATION of the BRCA-1/BRCA-2 genes) may choose prophylactic mastectomy, also called risk-reduction mastectomy, to reduce the likelihood that they will develop cancer. Mastectomy is a major surgery that may require two to five days of hospitalization after the operation, depending on the extent

of the surgery. Women may choose to have immediate or follow-up breast reconstructive surgery, or no reconstruction.

Surgical Procedure

A woman undergoing mastectomy receives general ANESTHESIA. The operation generally takes two to four hours; mastectomy with reconstruction takes longer than mastectomy alone. There are three types of mastectomy:

- Segmental mastectomy is when the surgeon removes the tumor and the quadrant of breast that contains it. The surgeon may recommend this operation when the breast cancer tumor is small and localized though larger than would be appropriate for lumpectomy (removal of the tumor and a margin of the surrounding breast tissue).
- Subcutaneous mastectomy, also called SKIN-sparing mastectomy, is removal of the breast tissue with the nipple, areola, and surface skin of the breast remaining. Subcutaneous mastectomy affords the most ideal circumstance for breast reconstruction.
- Total mastectomy, also called simple mastectomy, removes all of the breast tissue including the nipple and areola. The surgeon may recommend total mastectomy when the cancer is diffuse (lacking clear boundaries) or in more than one location within the breast. The surgeon may also perform SENTINEL LYMPH NODE DISSECTION, a method that examines the first LYMPH NODE in the drainage path from the tumor. Whether the sentinel contains cancer cells is an accurate indicator of whether the cancer has spread from the breast.
- Modified radical mastectomy removes all of the breast, including the nipple and areola, as well as the axillary LYMPH nodes (lymph nodes under the arm), called axillary lymph node dissection. This is the operation of choice when the cancer tumor is fairly large or diagnostic scans show the lymph nodes contain cancer.

After removing the breast the surgeon places small tubes to drain fluid from the surgical site during the initial stages of HEALING and then sutures closed the surgical incision. The surgeon removes the drains three to seven days after the operation, usually before the woman leaves the hospital. The nature and extent of scarring and deformity depends on the type of mastectomy. If there are skin sutures, they are usually ready for removal in five to seven days.

Risks and Complications

As with any surgery, the risks of mastectomy include excessive bleeding, INFECTION, and reaction to the anesthesia. These risks are slight. The potential for complications increases with the complexity of the surgery. Women who undergo modified radical mastectomy with axillary lymph node dissection may have significant swelling in the arm on the side of the surgery in the immediate postoperative recovery period as well as intermittently over the long term. Many women undergo adjuvant therapy (follow-up treatment), such as RADIATION THERAPY or CHEMOTHERAPY, after mastectomy for breast cancer. These therapies carry their own risks and do not usually affect the course of healing from the surgery.

Outlook and Lifestyle Modifications

With early detection and treatment, recovery from both the mastectomy and the breast cancer is complete. Recovery from modified radical mastectomy can take several months, with restrictions on lifting and some physical activities until the area fully heals and swelling (LYMPHEDEMA) is under control. It is difficult to predict who will have ongoing lymphedema; this is a significant long-term risk for any woman whose surgery includes axillary lymph node dissection. Women who choose not to have reconstructive surgery may opt instead for prosthetic bras. Many women have concerns about body image and sexuality; these are potentially significant issues that can affect QUALITY OF LIFE. Some women find SUPPORT GROUPS helpful.

See also CANCER TREATMENT OPTIONS AND DECISIONS; HORMONE-DRIVEN CANCERS; PAGET'S DISEASE OF THE BREAST; PLASTIC SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

mastitis INFLAMMATION of the BREAST, typically due to bacterial INFECTION. Mastitis usually begins as a combination of events: a blocked milk duct in

the breast of a woman who is BREASTFEEDING an infant and cracks or breaks in the SKIN, usually around the nipple, that allow BACTERIA to enter the milk duct. Mastitis due to infection is less common in women who are not breastfeeding. Mastitis may also occur as a result of viral infection or become chronic for reasons the doctor cannot identify though are likely hormonal.

Bacterial Mastitis

The symptoms of bacterial mastitis include PAIN, redness on the skin above the area of the infection, and swelling or hardness at the site of the infection. Many women also have FEVER, chills, bodywide MUSCLE aches, and fatigue. It is important for breastfeeding women to continue breastfeeding, as the infant's sucking helps massage the blockage from the duct. Warm compresses or a heating pad to the breast also may help.

A course of treatment with an antibiotic medication generally results in rapid improvement of bacterial mastitis. The small amount of the antibiotic that enters the breast milk is not enough to affect the infant. The doctor may recommend an analgesic medication to relieve pain and fever. A complication of bacterial mastitis is breast ABSCESS, in which the infection forms a pocket within the breast tissue that requires minor surgery to open and drain, as well as a more extended course of antibiotics, so HEALING can take place.

ANTIBIOTIC MEDICATIONS TO TREAT BACTERIAL MASTITIS

amoxicillin-clavulanic acid	cephalexin
ciprofloxacin	clindamycin
cloxacillin	flucloxacillin

Nonbacterial Mastitis

Mastitis may also result from viral infection, most commonly as a result of the MUMPS VIRUS. Nonspecific chronic mastitis sometimes occurs in a pattern that follows a woman's MENSTRUAL CYCLE, suggesting it is hormonal in nature. The diagnostic path for nonbacterial mastitis often includes MAMMOGRAM (X-RAY of the breasts) and sometimes biopsy of an area of inflammation to rule out BREAST CANCER or other causes for the symptoms. When such findings are negative, treatment is generally NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to relieve inflammation and pain. NSAIDs also influence the production and release of PROSTAGLANDINS, hormonelike substances that fluctuate in the BLOOD circulation during the menstrual cycle. Chronic mastitis is a common symptom of FIBROCYSTIC BREAST DISEASE.

See also ANALGESIC MEDICATIONS; ANTIBIOTIC MEDICATIONS; HORMONE; MASTALGIA.

masturbation Touching one's own body, and in particular the genitals, for sexual pleasure and typically to reach ORGASM. Masturbation is a normal behavior most common among adolescents and young adults. Masturbation does not cause adverse health effects, either of the genitals or health in general. For several centuries myths have persisted that masturbation causes blindness, mental illness or insanity, HAIR growth on the palms of the hands, INFERTILITY, and other problems. These myths arise from social and cultural attitudes toward masturbation, not from medical science. Excessive masturbation may indicate underlying psychologic or emotional conditions. Inappropriate masturbation (notably public masturbation) is often an indication of serious mental illness, DEMENTIA, or BRAIN damage (such as due to STROKE or trauma), conditions that disturb the normal inhibitory mechanisms of conscious behavior.

See also SEXUAL DYSFUNCTION; SEXUAL INTERCOURSE.

menarche A woman's first menstrual period, the start of MENSTRUATION and the beginning of FERTILITY. The average age of menarche varies among cultures and countries throughout the world and largely correlates with nutritional well-being. In the United States the average age of menarche is 12½; in rural regions of South Africa the average age of menarche is near age 14. The age of menarche has declined worldwide by nearly a year over the past century, which health experts believe reflects improved nutrition and overall health status. Many cultures celebrate menarche as a rite of passage that ushers a girl into womanhood.

See also AMENORRHEA; MENOPAUSE; MENSTRUAL CYCLE.

menopause A woman's last menstrual period, the end of MENSTRUATION and the closure of a

woman's FERTILITY. Though researchers understand the cascade of physiologic events that results in menopause, the triggering factors remain a mystery though many researchers believe a key triggering mechanism is the loss of viable eggs (ova). Doctors consider a woman to have reached menopause when she has experienced one continuous year (12 contiguous months) without menstrual periods. However, the common perception of menopause encompasses the period of time, often years, preceding menopause. Some people call this time PERIMENOPAUSE ("around menopause").

Though menopause is a natural life shift, not a health condition or disorder, many women experience discomforts as their bodies rebalance after HORMONE levels shift. Most notable among these discomforts are HOT FLASHES, irregular menstrual periods or abnormal vaginal bleeding, and mood changes. Not all women experience all or even any of these discomforts; some women experience additional or different discomforts such as joint pain and HEADACHE. The transition of menopause is a uniquely individual passage.

Indications of Menopause

The most defining indication of menopause is the discontinuation of menstruation. In most women this occurs as a gradual process during which menstrual periods become increasingly irregular both in timing and quality. A woman may have three periods that are three weeks apart and last eight or nine days each, have one three-day period six weeks later, then not have another period for four months. This pattern may extend over three to five years, during which a woman typically experiences other indications that her hormone levels are fluctuating and dropping. Such indications commonly include

- vaginal dryness and painful sexual intercourse
- hot flashes and night sweats
- tendency to cry, mood swings, and irritability
- difficulty sleeping
- diminished ability to concentrate and memory difficulties
- decreased LIBIDO (sex drive)
- anxiety or DEPRESSION

Some women barely notice any of these indications and other women find that they interfere with nearly all aspects of their lives. There are few clinical answers to explain the broad range of experience, nor to predict what course a particular woman's menopause experience will take. There is some indication that a woman tends to have an experience similar to her mother's, though whether the reasons are cultural or physiologic remains unknown.

Relieving Menopause Discomforts

There are numerous approaches to relieving the discomforts of menopause, some of which are clinical and others that are alternative and lifestyle. The more a woman understands the changes that are occurring in her body and the natural course they represent, the more effectively she can cope with their effects and choose methods of relief that are appropriate for her health status and her degree of discomfort. Many women find the most effective solutions involve a mix of methods, and that the mix changes as menopause progresses.

Hormone replacement therapy (HRT) For the last half of the 20th century doctors treated menopause with hormone replacement therapy (HRT), hormone supplementation to elevate the levels of ESTROGENS and PROGESTERONE in the BLOOD circulation. The intent of HRT was to bring up these levels enough to relieve discomforts without restoring the menstrual cycle. Doctors also believed HRT helped protect a woman from CARDIOVASCULAR DISEASE (CVD) and OSTEOPOROSIS, two conditions that can have dire consequences as a woman ages. The foundation for this belief was the sharp rise in incidence of HEART ATTACK and the high rate of osteoporosis among women after menopause who did not take HRT. It seemed that women who took HRT were less likely to have either condition. Many American women took HRT for the last half of their lives.

However, extensive clinical studies began to show in the early 2000s that contrary to these popular perceptions, HRT did not have a protective effect against CVD and had perhaps a limited protective benefit for osteoporosis. Further, HRT significantly increased the risk for some types of HORMONE-DRIVEN CANCERS, such as BREAST CANCER and ENDOMETRIAL CANCER. In 2002 health agencies

withdrew recommendations for routine long-term HRT, advising that doctors instead prescribe time-limited hormone supplementation to relieve menopausal discomforts only when they interfered with a woman's QUALITY OF LIFE. Under the current standard of practice guidelines most women should not take hormone supplementation for longer than two years, with a trial off the supplementation every six months to assess whether it remains necessary. Each woman's individual health circumstances require her doctor's careful evaluation to determine whether hormone supplementation is appropriate.

There is a sizable group of health-care professionals who prescribe BIHRT (bio-identical hormone replacement therapy). BIHRT utilizes hormones such as estradiol, progesterone, and testosterone that are chemically identical to those found in the woman's body. It is felt by many that not only do they not pose the same health risks as were identified in the WHI study but do actually provide numerous health benefits.

Nonhormonal approaches Selective serotonin reuptake inhibitors (SSRIs), a class of ANTIDEPRESSANT MEDICATIONS, have emerged as effective therapies to relieve hot flashes. Doctors usually prescribe these medications at doses lower than those typically used to treat depression. Researchers do not know the precise mechanisms through which SSRIs relieve hot flashes.

There are numerous alternative or complementary approaches to relieve menopausal discomforts, some of which show evidence of their success through clinical studies. Among them include ACUPUNCTURE, SOY, and the medicinal herb BLACK COHOSH, all to relieve hot flashes, and wild yam cream to relieve vaginal dryness. Soy and black cohosh contain PHYTOESTROGENS, plant-based substances that are similar to human estrogens and bind with estrogen receptors in the body, though with less intensity than endogenous estrogens. Wild yams contain a plant-based form of progesterone.

Other remedies are widely believed to provide relief but lack evidence, either because studies have not been done or have produced inconclusive or conflicting results. Among these are black cohosh to relieve mood swings and irritability and DONG QUAI, soy, and red clover to relieve hot flashes and other discomforts. Evening primrose oil and vitamin E supplements appear to help with relaxation and sleep.

ALTERNATIVE REMEDIES TO TREAT MENOPAUSAL DISCOMFORTS

ACUPUNCTURE	BLACK COHOSH
DONG QUAI	evening primrose oil
red clover	SOY
vitamin E	progesterone cream

Changes That Occur with Menopause

Estrogen has multiple and powerful actions in a woman's body and the decline of its presence after menopause results in changes that affect all body systems. One such action is a diminished ability to repair collagen structures in the body such as ligaments, tendons, and the SKIN. The loss of collagen may affect the ligaments in the abdomen that support the UTERUS, particularly in women who have given birth, resulting in UTERINE PROLAPSE. A good number of women experience URINARY INCONTINENCE as a result of weakening of the muscles that control the flow of URINE; KEGEL EXERCISES often improve or prevent this. The skin thins and becomes less elastic, resulting in wrinkles. Sebaceous secretions also diminish, causing the skin to become dry. The mucous lining of the VAGINA thins as well, resulting in reduced vaginal secretions. The more fragile vagina may produce symptoms such as burning and itching (VAGINITIS) and discomfort during SEXUAL INTERCOURSE.

Changes in collagen also affect the walls of the arteries, causing them to become less flexible and less able to relax (dilate). As well, estrogen plays a key role in the METABOLISM of cholesterol and fatty acids. As estrogen levels drop the body handles these lipids less efficiently. Consequently HYPERLIPIDEMIA, ATHEROSCLEROSIS, and HYPERTENSION (high BLOOD PRESSURE) become more common after menopause. In addition, loss of estrogen (specifically estradiol) can contribute to HYPOTHYROIDISM and increased CORTISOL potentially leading to INSULIN RESISTANCE. Estrogen also acts as a natural selective serotonin reuptake inhibitor (SSRI) so its loss contributes to increased DEPRESSION. Nutritious EATING HABITS and daily physical exercise become especially important to maintain cardiovascular health in light of these changes.

Estrogen is also essential for maintaining the content of calcium and other bone-building minerals. After menopause calcium more easily leaves the bones and is less easily absorbed into the blood circulation from dietary sources, a double effect that can rapidly result in osteoporosis. More than two thirds of women over age 65 have some degree of osteoporosis. Calcium supplementation in combination with RESISTANCE EXERCISE (also called weight-bearing exercise) helps the bones to retain the calcium they require to remain dense and strong.

See also AMENORRHEA; BONE; BONE DENSITY; CHOLESTEROL, ENDOGENOUS; EXERCISE AND HEALTH; GENERAL ANXIETY DISORDER (GAD); HYSTERECTOMY; MEDICINAL HERBS AND BOTANICALS; MENARCHE; PREMATURE OVARIAN FAILURE (POF).

menstrual cramps See DYSMENORRHEA.

menstrual cycle The pattern of hormonal and physiologic changes that occur that occur in a woman's body in preparation for possible PREGNANCY. Though the average menstrual cycle spans 28 days, the frequency of MENSTRUATION varies widely among women and often within each woman individually. Menstrual cycles may be as short as 25 days or as long as 32 days and still be within the range of normal. Menstrual cycles outside these parameters may or may not be normal, depending on the woman's individual physiology and health status. The endocrine system directs the menstrual cycle.

Physiologic Phases of the Menstrual Cycle

There are four phases within the menstrual cycle that always occur in the same order:

1. The proliferative phase begins with the end of menstruation and the return of the endometrium (lining of the UTERUS) to its nonmenstrual state and culminates with OVULATION about 14 days after the onset of menstruation. During proliferation the level of ESTROGENS in the BLOOD circulation rises and the level of PROGESTERONE drops. The changing hormone levels stimulate the maturation of up to 20 ova within their ovarian follicles, called ripening. The follicle containing the first ovum to reach full maturity ruptures and releases the ovum into the fluid surrounding the fimbriae (fluted edges) of the fallopian tube. The other follicles that had started to develop then shrink; the ovary absorbs them and their ova.
2. The expelled ovum leaves behind the corpus luteum, a structure of endocrine tissue that begins secreting estrogens and progesterone. This period of activity by the corpus luteum is the luteal phase, also called the secretory phase. The increased blood levels of the hormones cause the endometrium to thicken and its blood vessels to enlarge. The glands that line the endometrium increase their secretions, and the inner endometrium becomes spongy and engorged in preparation to support implantation should CONCEPTION occur. The luteal phase lasts about 10 days.
3. When the ovum passes through the uterus without implanting, the corpus luteum involutes (turns in on itself) and the follicle absorbs it. The sudden drop in estrogens and progesterone causes the endometrial blood vessels to contract, called endometrial ischemia. The endometrial glands stop their secretions and the endometrium dramatically shrinks. This third phase of the menstrual cycle, called the ischemic phase, lasts 36 to 48 hours.
4. The culminating phase of the menstrual cycle is menstruation, during which the anemic (blood-deprived) tissue of the endometrium sloughs away and passes from the body. The menstrual flow contains tissue fragments, endometrial secretions, and blood. Menstruation lasts 3 to 5 days in 85 percent of women; about 15 percent of women menstruate for 7 days. Though menstruation is the last phase of the menstrual cycle, doctors consider the first day of menstrual bleeding to be the start of the menstrual cycle.

Endocrine Regulation of the Menstrual Cycle

The HYPOTHALAMUS, PITUITARY GLAND, and corpus luteum regulate the menstrual cycle. The hypothalamus initiates the proliferative phase of the menstrual cycle by releasing GONADOTROPIN-RELEASING HORMONE (GNRH). GnRH stimulates the pituitary gland to secrete a surge of FOLLICLE-STIMULATING

HORMONE (FSH), which induces an ovarian follicle to begin secreting estrogens. The estrogens cause the ovum within the follicle to begin ripening. The rising level of estrogens in the blood circulation triggers the hypothalamus to again release GnRH, which this time stimulates the pituitary gland to secrete LUTEINIZING HORMONE (LH). LH causes the ovarian follicle to produce progesterone, which brings the ovum to maturity and release (ovulation). Without pregnancy the blood levels of estrogens and progesterone both fall and menstruation takes place.

Disturbances of the Menstrual Cycle

Numerous factors may disrupt the menstrual cycle, the most common being pregnancy. When a fertilized ovum (ZYGOTE) implants in the endometrium, the menstrual cycle ends and pregnancy begins. The menstrual cycle does not return until six to eight weeks (and sometimes longer, up to months in women who are breastfeeding) after CHILDBIRTH. Hormonal imbalances may also disrupt the menstrual cycle. HYPOTHYROIDISM (underactive THYROID GLAND) or HYPERTHYROIDISM (overactive thyroid gland) is a common source of such hormonal disruption. Disorders of the pituitary gland, such as pituitary ADENOMA, or the ADRENAL GLANDS, such as ADRENAL INSUFFICIENCY, often alter the body's endocrine matrix in ways that affect the menstrual cycle.

Numerous medications and treatments such as CHEMOTHERAPY and RADIATION THERAPY may affect ovarian function. Menstrual disturbances may occur as a result of underlying health conditions such as POLYCYSTIC OVARY SYNDROME (PCOS), OBESITY, anorexia, and extreme emotional or physical stress. Though a normal menstrual cycle often occurs with a single functioning ovary, the absence or loss of both OVARIES ends the menstrual cycle. OOPHORECTOMY is the surgical OPERATION to remove an ovary. Women who participate in intense athletic activities, such as marathons and triathlons, may have irregular menstrual cycles or AMENORRHEA (absence of menstruation).

For further discussion of the menstrual cycle within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System." For further discussion of the menstrual cycle within the context of the structures and functions of the endocrine system, please see the overview section "The Endocrine System."

See also DYSFUNCTIONAL UTERINE BLEEDING (DUB); DYSMENORRHEA; FALLOPIAN TUBES; FERTILITY; INFERTILITY; MENARCHE; MENOPAUSE; PREMATURE OVARIAN FAILURE (POF); PREMENSTRUAL SYNDROME (PMS).

menstruation The final phase of the MENSTRUAL CYCLE, commonly called the menstrual period or simply the period. Menstruation is the discharge of BLOOD and excess tissue that build up within the UTERUS as endometrium (the lining of the uterus) thickens and engorges with blood in preparation for the implantation of a fertilized ovum (ZYGOTE). When PREGNANCY does not occur, hormonal changes cause the lining to slough away, passing from the uterus and out of the body via the VAGINA. Typically a woman passes two to three ounces of blood and other fluids over the course of the three to seven days she menstruates. The menstrual flow is generally heaviest on the second through the fourth days. About 85 percent of women menstruate for four to five days; about 15 percent menstruate for six to seven days.

Women typically use disposable sanitary napkins (commonly called pads) or tampons to capture the menstrual flow. Pads have adhesive strips that attach them to underwear; tampons fit inside the vagina. It is important to change either pads or tampons every four to six hours to prevent overflow and maintain appropriate PERSONAL HYGIENE. Tampons may irritate the vaginal walls. Because a tampon may carry BACTERIA into the vagina when the woman inserts, tampon use involves a slight risk for TOXIC SHOCK SYNDROME, a potentially life-threatening INFECTION. Doctors recommend using pads at night and during other times when it might not be possible or practical for a woman to change her sanitary protection every four to six hours.

There are no health reasons for women to avoid their regular activities, including sports, bathing, and sexual activity if desired, during menstruation. Women may prefer to shower when menstruating. Washing the GENITALIA with gentle soap and warm water is important to cleanse any accumulated menstrual fluids from the genital tissues, which reduces the presence of

bacteria as well as improves comfort. Many women wear tampons during athletic activities such as bicycling, swimming, dancing, and running. However, a woman should not sit in the bath tub or in a hot tub while wearing a tampon because the combination of heat and inactivity may draw bacteria into the vagina via the tampon's removal cord, which extends from the vaginal opening. A woman should also change her tampon immediately after water activities such as swimming.

For further discussion of menstruation within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; AMENORRHEA; DYSMENORRHEA; MENARCHE; MENOPAUSE; OVA; PUBERTY.

miscarriage See ABORTION.

mittelschmerz Discomfort a woman may feel on one side of her lower abdomen around the time she ovulates. The word is German for "middle PAIN," a reference to the occurrence of the discomfort midway through the MENSTRUAL CYCLE. The discomfort is often a sharp, achy pain that most commonly lasts from 2 to 12 hours though may continue up to 48 hours. Some women find the discomfort shifts sides from one menstrual period to another and some women have discomfort always on the same side. The side of the pain does not necessarily indicate which ovary is releasing an ovum as ovarian pain may refer to the opposite side of the lower abdomen.

Doctors believe mittelschmerz results from irritation the released ovum and the fluids that surround it create in the abdominal cavity, or from the pressure of the ovarian follicle immediately before its rupture to release the ovum. Mittelschmerz is a normal part of the menstrual cycle for many women and does not signal any underlying health concerns, though a doctor should evaluate any changes that may occur in the nature of the discomfort.

See also OVA; OVARIAN CYST; OVULATION.

morning sickness The NAUSEA and VOMITING that may occur during PREGNANCY, notably in the first trimester though it may continue through the second trimester and occasionally for the duration of the pregnancy. The term morning sickness is a misnomer as the nausea may occur at any time, day or night. However, many women do experience the nausea of pregnancy primarily in the morning when they first awaken. Many women find certain odors, tastes, or even appearances of food act as triggers for morning sickness.

Though doctors do not know for certain what causes morning sickness, they believe it is a reaction to the multitude of hormonal changes rapidly taking place in the woman's body as the pregnancy establishes itself. The onset of morning sickness, typically at about six weeks into the pregnancy, correlates with the surge of human chorionic gonadotropin (hCG) that emerges from the newly formed PLACENTA. Morning sickness, though disruptive, is not harmful for the pregnancy unless it prevents the woman from drinking enough water to remain hydrated. Most weight gain in pregnancy occurs in the second and early part of the third trimesters, and most women are able to eat enough to remain well nourished.

Nonpharmaceutical remedies for morning sickness include

- gingerroot shavings or tea
- flat GINGER ale (made with real ginger)
- cola syrup (available in drugstores) or flat cola soda
- soda crackers (such as saltines)
- not mixing solids and liquids
- small meals eaten frequently throughout the waking hours, and small snacks when awake during the night, so there is always something in the STOMACH
- ACUPUNCTURE or acupressure (including motion sickness wristbands that apply pressure to acupuncture points for nausea)

If these efforts are unsuccessful and morning sickness interferes with normal eating and drinking, the doctor may recommend or prescribe ANTIEMETIC MEDICATIONS that are safe to take during pregnancy. Some women experience relief with vitamin B_6 supplement, though doctors are unsure why this is. Because some medications may be

harmful to, or have unknown effects on, the developing FETUS, it is important to talk with the doctor before taking any medication or herbal remedy.

The doctor may consider intravenous fluids and nutrition for women who experience severe, extended morning sickness (called hyperemesis gravidarum), though the need for such intervention is uncommon. Morning sickness is more common in women who have a history of migraine HEADACHE, motion sickness, or morning sickness in previous pregnancies. Morning sickness is also more common in women who are pregnant with multiples (twins or higher).

See also PRENATAL CARE; VITAMINS AND HEALTH.

nabothian cyst A mucous-filled growth that develops within a nabothian gland. The nabothian glands are clusters of mucous-secreting cells on the surface of the CERVIX. Nabothian cysts are very common, cause no symptoms, and present no health risk. Typically the health-care provider discovers nabothian cysts, which are hard and pimplelike, during routine PELVIC EXAMINATION. Occasionally the doctor may choose to further examine nabothian cysts using COLPOSCOPY to confirm the diagnosis.

See also BARTHOLIN'S CYST; PAP TEST.

neonatal jaundice A condition in which the newborn infant's LIVER cannot yet properly destroy old erythrocytes (red BLOOD cells), resulting in the accumulation of BILIRUBIN in the blood circulation. The excessive bilirubin, a pigmented protein compound, gives the SKIN a characteristic yellowish orange hue. Neonatal JAUNDICE, also called physiologic jaundice of the newborn, is more common in infants born before 37 weeks gestational age because of the immaturity of their livers.

Mild neonatal jaundice clears on its own within a few days. The doctor may prescribe photolight therapy (also called PHOTOTHERAPY) for moderate neonatal jaundice, a treatment that exposes the infant's skin to short periods of ultraviolet light. Ultraviolet light expedites the chemical breakdown of the bilirubin so the body can excrete it.

Circumstances of jaundice in a newborn may result from numerous pathologic causes including BILIARY ATRESIA (absence of the BILE DUCTS), BOWEL ATRESIA (absence of the large intestine), hemolytic disease of the newborn (Rh incompatibility), and congenital HEPATITIS B.

See also ANEMIA; BLOOD TYPE; ERYTHROCYTE.

nocturnal emission ORGASM and EJACULATION that occur when a boy or man is asleep. Nocturnal emissions are natural and normal across the age spectrum from ADOLESCENCE through old age, though are most common during adolescence when SECONDARY SEXUAL CHARACTERISTICS are developing and HORMONE levels are rising. Researchers believe nocturnal emissions often occur during dreams (thus the casual term "wet dreams") though the man may not remember dreaming.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; MASTURBATION; PUBERTY; SEXUAL HEALTH.

oophorectomy A surgical OPERATION to remove one ovary (unilateral oophorectomy) or both OVARIES (bilateral oophorectomy) in a woman. Oophorectomy may be therapeutic (to treat a health condition) or prophylactic (to prevent a health condition).

The key health conditions for which therapeutic oophorectomy is an option include OVARIAN CANCER, severe ENDOMETRIOSIS, ovarian ABSCESS (INFECTION of the ovary), and large or multiple ovarian cysts. Prophylactic oophorectomy is an effort to lower the possibility for developing HORMONE-DRIVEN CANCERS (ovarian, breast, endometrial) in a woman who has unusually high risk for such cancers, either genetically or because of a prior such cancer. Removing both ovaries cuts a woman's estrogen production to almost nothing, mostly depriving hormone-sensitive cancer cells of the substance they require to thrive.

Unilateral oophorectomy often allows a woman to preserve her FERTILITY because the remaining ovary, if healthy, continues to produce hormones and OVA (eggs) that maintain the MENSTRUAL CYCLE. Bilateral oophorectomy entirely ends ovarian function and the menstrual cycle, resulting in abrupt MENOPAUSE in women who are still menstruating at the time of surgery. Such surgically induced menopause, because it is sudden, may thrust the body into significant symptoms such as HOT FLASHES.

The operation for either unilateral or bilateral oophorectomy may be OPEN SURGERY, in which the surgeon makes an incision in the lower abdomen large enough to expose the ovary, or MINIMALLY INVASIVE SURGERY, in which the surgeon makes several small incisions in the lower abdomen and visualizes the operative site using a laparoscope. The type of operation depends on multiple factors including the reason for the oophorectomy and the woman's general health status. Open oophorectomy requires three to five days of hospitalization and six to eight weeks for recovery. Laparoscopic oophorectomy is often an ambulatory (outpatient) surgery with rapid recovery and return to regular activities within a week or two. About half of total hysterectomies (operations to remove the UTERUS) also include removal of the ovaries (hystero-oophorectomy) or the ovaries and the FALLOPIAN TUBES (hysterosalpingo-oophorectomy).

The short-term risks of oophorectomy include excessive bleeding and postoperative infection. The key long-term complication of bilateral oophorectomy is OSTEOPOROSIS (loss of BONE DENSITY), the risk for which arises from the depletion of estrogen.

See also BRCA-1/BRCA-2; BREAST CANCER; CANCER TREATMENT OPTIONS AND DECISIONS; CA-125; ENDOMETRIAL CANCER; HYSTERECTOMY; LASER SURGERY; MINIMALLY INVASIVE SURGERY; ORCHIECTOMY; OVARIAN CYST; SURGERY BENEFIT AND RISK ASSESSMENT.

orchiectomy A surgical OPERATION to remove one testicle (unilateral orchiectomy) or both TESTICLES (bilateral orchiectomy) in a man. Unilateral orchiectomy is typically a treatment for TESTICULAR CANCER or severe TESTICULAR TORSION in which the testicle becomes gangrenous due to prolonged loss of BLOOD circulation. Bilateral orchiectomy is typically a treatment for advanced PROSTATE CANCER.

The testicles produce both TESTOSTERONE and SPERM. Many men who undergo unilateral orchiectomy retain their FERTILITY and full sexual function. However, other treatment such as CHEMOTHERAPY may affect sperm production and thus fertility. Bilateral orchiectomy ends produc-

tion of both testosterone and sperm, resulting in permanent INFERTILITY. The intent of bilateral orchiectomy is to cut the supply of testosterone that feeds prostate cancer cells, as prostate cancer is one of the HORMONE-DRIVEN CANCERS. The resulting precipitous decline in testosterone production often also diminishes LIBIDO (sex drive) and may cause ERECTILE DYSFUNCTION (difficulty achieving or sustaining an ERECTION).

For unilateral orchiectomy the surgeon removes the testicle through an incision in the lower abdomen, just above the pubic HAIR line. The incision exposes the inguinal canal, a passage of ligaments through which the testicles originally descended into the SCROTUM. The surgeon manipulates the testicle upward from the scrotum into the lower abdomen, extracting it through the incision. This procedure prevents damage to the scrotum that could allow cancer cells to escape into the LYMPH nodes; the testicles and the scrotum use different lymph networks so the surgeon does not want to disturb the scrotum or create a circumstance in which cells from the testicle can enter the lymph nodes that serve the scrotum. For bilateral orchiectomy as prophylactic treatment for advanced prostate cancer the surgeon may make the incision in the scrotum.

The key risks of orchiectomy include excessive bleeding and INFECTION. Unilateral orchiectomy sometimes lowers testosterone levels, which the doctor may treat with testosterone supplementation. Long-term complications that occur with bilateral orchiectomy include loss of BONE DENSITY and increased risk for OSTEOPOROSIS, GYNECOMASTIA (enlarged breasts), and erectile dysfunction.

See also GANGRENE; OOPHORECTOMY; ORCHIOPEXY; SURGERY BENEFIT AND RISK ASSESSMENT.

orchiopexy A surgical OPERATION to correct an undescended testicle (CRYPTORCHIDISM). Nearly always the operation takes place early in childhood, typically between ages six and 12 months. In many situations the operation is an outpatient procedure the surgeon can perform in an AMBULATORY SURGICAL FACILITY, usually with general ANESTHESIA.

The surgeon makes two incisions, one in the lower abdomen and one in the SCROTUM. The abdominal incision provides access to the undescended testicle, which the surgeon manipulates through the inguinal canal (a passageway through the ligaments supporting the pelvic floor) and into the scrotum. Through the incision in the scrotum the surgeon sutures (stitches) the testicle to the inside of the scrotum so it cannot reascend.

The primary risks of orchiopexy are excessive bleeding and INFECTION, both of which are uncommon. Recovery is typically rapid, with HEALING complete within two weeks. When done early in childhood, orchiopexy preserves FERTILITY. However, an increased risk for TESTICULAR CANCER remains, making TESTICULAR SELF-EXAMINATION an important screening procedure.

See also ORCHIECTOMY; SURGERY BENEFIT AND RISK ASSESSMENT; TESTICLES.

orchitis INFLAMMATION of one testicle or both TESTICLES, often due to INFECTION. Bacterial infection may result from SEXUALLY TRANSMITTED DISEASES (STDS) such as GONORRHEA or SYPHILIS. MUMPS, a viral INFECTION that primarily affects the SALIVARY GLANDS, is a common cause of orchitis, particularly when the mumps VIRUS infects adult men.

The symptoms of orchitis are PAIN and swelling of the involved testicle. The diagnostic path includes physical examination of the SCROTUM and testicles and sometimes ULTRASOUND to rule out other causes of similar symptoms such as TESTICULAR TORSION, HYDROCELE, or VARICOCELE.

Treatment with ANTIBIOTIC MEDICATIONS is necessary when the infection is bacterial. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) relieve pain and inflammation regardless of the cause. Resting in a reclining position or wearing an athletic supporter also provides relief. A complication of orchitis may be testicular atrophy (reduced size of the affected testicle), which may affect SPERM production and FERTILITY. An atrophied testicle also presents an increased risk for TESTICULAR CANCER, making routine TESTICULAR SELF-EXAMINATION prudent.

See also BACTERIA; EPIDIDYMITIS.

orgasm Intense sensation of pleasure and excitement that occurs at the culmination of sexual stimulation. Involuntary contractions of the pelvic muscles typically accompany orgasm. In men these contractions result in EJACULATION, propelling SEMEN from the urethral opening (meatus) at the

tip of the PENIS. In women the contractions of orgasm occur as rhythmic waves along the walls of the VAGINA. Aside from being a source of intense pleasure, orgasm appears to serve as a mechanism to facilitate the movement of SPERM through the vagina. This is important from a reproductive perspective as the vagina presents a fairly hostile environment for sperm, which are not able to survive longer than an hour or two within it.

Though a man can have an orgasm without ejaculating, he cannot ejaculate without orgasm. After orgasm a man enters a refractory period during which his body recovers from the experience. During this time the mechanism of ERECTION does not respond to sexual stimulation and many men feel the overwhelming desire to fall asleep. The length of the refractory period varies with age and among men, ranging from 10 to 20 minutes for a man in his 20s to an hour or longer for a man 50 or older. A woman does not have a refractory period and may continue or revive sexual arousal indefinitely. The consistent inability to reach orgasm is a form of SEXUAL DYSFUNCTION that may have physiologic or emotional foundations.

See also ERECTILE DYSFUNCTION; MASTURBATION; RETROGRADE EJACULATION; SEXUAL INTERCOURSE.

ova The female cells of reproduction, also called eggs or gametes. An ovum, also called an oocyte (single egg cell), is a haploid cell; it contains one half of the genetic material necessary for human life. At birth the OVARIES contain about 400,000 follicles, each of which holds a single immature ovum. At PUBERTY the follicles begin to ripen, with usually one ovum coming to maturity with each MENSTRUAL CYCLE. Over the course of a woman's reproductive years her ovaries produce 400 to 600 ripened ova. About 10 to 20 times as many ova begin but do not complete the maturation process. The ovaries eventually absorb ova that fail to reach maturity.

Ovulation The sequence of hormonal and physiologic changes that bring an ovum to maturity is OVULATION, which takes place during the start of the menstrual cycle's luteal phase around day 14 of the menstrual cycle (day 1 being the first day of MENSTRUATION). The PITUITARY GLAND releases first a surge of FOLLICLE-STIMULATING HORMONE (FSH), which activates an ovarian follicle. The follicle secretes ESTROGENS, which begin the maturation process for the ovum the follicle contains. The pituitary gland then secretes LUTEINIZING HORMONE (LH), which induces the ovarian follicle to produce PROGESTERONE. The progesterone brings the ovum to full maturity and the follicle ruptures, releasing the ovum for capture into the fallopian tube.

Fertilization, implantation, and conception The smooth MUSCLE walls of the fallopian tube contract in a gentle, wavelike pattern that draws the ovum through the tube toward the UTERUS. When SPERM are also present in the fallopian tube, fertilization takes place. Typically, though many sperm attempt to penetrate the outer membrane of the ovum only one succeeds. The chemical composition of the ovum's membrane alters once the sperm is within the ovum, preventing other sperm from following. The nuclei of the gametes (ovum and sperm) fuse to form a single diploid cell, called a ZYGOTE. As the zygote moves along the fallopian tube toward the uterus it continues to grow and divide. By the time the zygote reaches the uterus it has become a two-layered mass of cells called a blastocyst. The outer layer of the blastocyst attaches to the endometrium; as pregnancy continues this layer becomes the PLACENTA and the inner layer develops into the EMBRYO. The completion of fertilization and implantation is CONCEPTION.

For further discussion of the ova within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); CELL STRUCTURE AND FUNCTION; FALLOPIAN TUBES; FERTILITY; GAMETE; INFERTILITY; PREGNANCY; SECONDARY SEXUAL CHARACTERISTICS; SEXUAL HEALTH.

ovarian cancer A malignant (cancerous) tumor that develops in the tissues of the ovary. Ovarian cancer may arise from any of the ovary's three types of cells—germ, stromal, and epithelial—though about 90 percent of ovarian cancers arise from the ovarian epithelium (the membranous covering of the ovary). Ovarian epithelial cancer occurs most commonly in women over age 60 (after MENOPAUSE). Though tumors are typically noncancerous or cancerous, ovarian epithelial

tumors may straddle the border. Doctors classify such tumors as low malignant potential (LMP); though cancerous these tumors grow slowly, have little propensity to metastasize (spread) and usually respond very well to treatment. Ovarian epithelial cancer that develops in women under age 60 is often LMP. Ovarian germ cell cancer and ovarian stromal cell cancer are rare; they are more likely to occur in women under age 50 (before menopause).

Doctors in the United States diagnose ovarian cancer in about 22,000 women each year. Because ovarian cancer typically causes few symptoms until it has metastasized (spread), the prognosis (outlook) for ovarian cancer overall is rather bleak. However, early diagnosis allows successful treatment and a promising outlook. Any woman who has her OVARIES is vulnerable to ovarian cancer, even if she has had a HYSTERECTOMY (OPERATION to remove the UTERUS). Bilateral OOPHORECTOMY (operation to remove both ovaries) ends the risk for ovarian cancer, though it remains possible for epithelial cancer very much like ovarian cancer to develop in the peritoneum, the membranous lining of the abdominal cavity.

Symptoms and Diagnostic Path

Early symptoms of ovarian cancer are often generalized and vague. Both the woman and her doctor commonly mistake them for symptoms of gastrointestinal disorders. These early symptoms may include

- sensation of abdominal bloating
- abdominal swelling
- unexplained weight gain
- changes in bowel habits (CONSTIPATION or DIARRHEA)
- urinary urgency

As ovarian cancer progresses, symptoms become more specific and include

- pelvic, abdominal, or low BACK PAIN
- unexplained weight loss
- unusual vaginal bleeding
- fatigue and general sense of not feeling well (malaise)
- persistent gastrointestinal symptoms (NAUSEA, VOMITING, diarrhea, or constipation) that do not vary with eating patterns

The diagnostic path includes comprehensive medical examination including PELVIC EXAMINATION, BLOOD tests (cell count and differentiation as well as CA-125), abdominal ULTRASOUND or COMPUTED TOMOGRAPHY (CT) SCAN, and often COLONOSCOPY.

Blood levels of the protein CA-125 are often elevated in moderate to advanced ovarian cancer though not in early ovarian cancer. As well, numerous noncancerous conditions can elevate CA-125 blood levels. Though the doctor may consider the CA-125 level among the diagnostic indicators, it does not alone confirm or rule out diagnosis of ovarian cancer. Other tumor markers include ALPHA-FETOPROTEIN (AFP), HUMAN CHORIONIC GONADOTROPIN (hCG), and CARCINOEMBRYONIC ANTIGEN (CEA).

Because benign tumors and cysts of the ovaries are common, noninvasive diagnostic procedures often cannot determine whether an ovarian growth is cancerous or noncancerous. The only certain diagnostic procedure is laparoscopy or laparotomy, both of which are surgical operations to enter the abdominal cavity, to view the ovary and remove samples of tissue (biopsy). Laparoscopy is a MINIMALLY INVASIVE SURGERY in which the surgeon uses several small incisions through which he or she inserts an endoscope (flexible, lighted viewing instrument) and specialized instruments to visualize the ovary via display on a monitor. Laparotomy is an OPEN SURGERY in which the surgeon makes a substantial incision through the SKIN in the abdomen and examines the ovary directly.

The pathologist who examines the tissue samples determines the type of cancer cells that are present and assesses the extent to which they are likely to have spread to locations outside the ovary. The results of this assessment, called STAGING AND GRADING OF CANCER, help guide treatment decisions. The pathologist also may revise the stage or grade may change after surgery to remove the cancer, depending on the surgeon's findings and the character of the cancer cells within the tumor.

BASIC STAGING OF OVARIAN CANCER

Stage	Meaning	Treatment Options
low malignant potential (LMP)	tumor is borderline cancerous and slow growing	surgery to remove the involved ovary (unilateral OOPHORECTOMY)
stage 1	cancer remains confined to a local tumor in one ovary	surgery (bilateral salpingo-oophorectomy, total HYSTERECTOMY, omentectomy, and lymphadenectomy) intraperitoneal CHEMOTHERAPY, RADIATION THERAPY with follow-up single DRUG chemotherapy, or combination (multiple drug) chemotherapy
stage 2	cancer involves both OVARIES or has spread to the FALLOPIAN TUBES, UTERUS, or tissue within the pelvis	surgery (bilateral salpingo-oophorectomy, total hysterectomy, omentectomy, and LYMPH NODE dissection) combination chemotherapy, four to six cycles
stage 3	cancer has spread to other organs in the abdomen, the peritoneum, and abdominal LYMPH nodes	surgery (bilateral salpingo-oophorectomy, total hysterectomy, omentectomy, and lymph node dissection) and debulking surgery combination chemotherapy, four to six cycles
stage 4	cancer has spread to distant organs	debulking surgery combination chemotherapy, multiple cycles "second look" surgery to remove remaining cancerous tissue
stage 4/recurrent	cancer has returned after treatment	combination chemotherapy IMMUNOTHERAPY clinical trial of appropriate investigational new treatments high-DOSE chemotherapy with autologous bone marrow therapy (STEM CELL support) palliative surgery for symptom relief

Treatment Options and Outlook

The treatment of first choice for nearly all ovarian cancers is surgery to remove the ovary that contains the tumor. In all ovarian cancers except LMP, surgery also includes removal of the rest of the pelvic reproductive organs—both ovaries, both FALLOPIAN TUBES, uterus, and CERVIX—as well as the omentum (a layer of fatty tissue that covers the interior of the peritoneum) and nearby LYMPH nodes (lymphadenectomy). Because ovarian cancer tends to spread in layers of cells that cover the pelvic or abdominal structures, the surgeon removes as much of it as possible through a procedure called debulking. Debulking may also involve removing segments of the SMALL INTESTINE.

Most women also receive adjuvant therapy (follow-up treatment) with CHEMOTHERAPY, RADIATION THERAPY, or both. Treatment with a single chemotherapy agent is often sufficient to treat early stage 1 ovarian cancer, though many oncologists prefer combination chemotherapy or radiation therapy with single-agent chemotherapy after. Multiple cycles of combination chemotherapy are the current standard of treatment for stage 2 through stage 4/recurrent ovarian cancer. Some chemotherapy agents are available in oral forms

(pills), which a woman can take at home, and others are available only in intravenous injectable forms, which require administration at a chemotherapy center.

CHEMOTHERAPY AGENTS TO TREAT OVARIAN CANCER	
cisplatin	doxorubicin
etoposide	ifosfamide
melphalan	paclitaxel
topotecan	

High-dose chemotherapy with autologous BONE MARROW therapy, also called STEM CELL support, is often effective in providing short-term REMISSION in stage 4 ovarian cancer. However, many cancer experts question whether the high risk and cost of this treatment ultimately improves a woman's QUALITY OF LIFE and LIFE EXPECTANCY. For many women, investigational treatments provide equal or better results with significantly less severe side effects and complications.

Because the spread of ovarian cancer within the abdominal cavity is so diffuse, early detection and treatment are particularly essential. Surgery is most effective when the tumor remains confined to the ovary; treatment is most effective when the surgeon is able to remove all of the cancer. The outlook for remission with early treatment is very good. Later stage ovarian cancer is difficult to control because the surgeon cannot remove all of the cancer. Chemotherapy provides highly effective treatment though side effects can be significant. Later stage ovarian cancer has a tendency to recur after remission, though each period of remission may last three to five years.

Risk Factors and Preventive Measures

The primary risk factors for ovarian cancer are age greater than 60 years and family history of ovarian cancer, especially among first-degree relatives (mother, daughter, sister). Women who carry the BRCA-1/BRCA-2 GENE mutations have especially high risk, though not the certainty, to develop ovarian cancer. Some women who have such high risk choose prophylactic oophorectomy (surgery to remove the ovaries) when they reach the end of their childbearing years or menopause as a means for reducing their risk.

The causes of ovarian cancer are unclear, though there appear to be hormonal correlations. Women who carry at least one pregnancy to delivery, breastfeed, or take oral contraceptives (birth control pills) for longer than three years, or have a TUBAL LIGATION or a total hysterectomy (surgery to remove the uterus and cervix) for reasons other than cancer appear significantly less likely to develop ovarian cancer. Lifestyle factors such as the fat content of the diet and the frequency of physical exercise also correlate to the risk for ovarian cancer, with the risk much lower in women who eat a low-fat diet and get daily physical exercise (minimum 30 to 60 minutes). Cigarette smoking raises the risk for ovarian cancer, as it does for many cancers.

Though many ovarian tumors are difficult to palpate (feel), health experts recommend routine pelvic examination as a means of possible early detection of ovarian cancer. However, the PAP TEST that often accompanies a pelvic examination, while very effective for detecting early CERVICAL CANCER, does not detect ovarian cancer. The schedule of examination varies with age and health status, though women at high risk for ovarian cancer should have annual pelvic examinations.

See also BREAST CANCER; CANCER TREATMENT OPTIONS AND DECISIONS; COLORECTAL CANCER; ENDOMETRIAL CANCER; ENDOSCOPY; SURGERY BENEFIT AND RISK ASSESSMENT.

ovarian cyst A noncancerous, fluid-filled growth that forms within an ovary. Ovarian cysts are common and many are transient (come and go). The most common type of ovarian cyst is a follicular cyst, which develops in an ovarian follicle. Typically the follicle fills with fluid. Over time the fluid reabsorbs into the follicle and the cyst goes away. Sometimes a follicular cyst ruptures, causing sudden PAIN. Cysts may also form in the corpus luteum, the structure of endocrine tissue that supports a ripened ovum. Such a cyst, called a luteal cyst, typically goes away when the corpus luteum involutes (turns in on itself) and becomes absorbed into the ovarian follicle immediately preceding MENSTRUATION. Follicular cysts and luteal cysts are usually functional—that is, they come and go with the hormonal shifts of the MENSTRUAL

CYCLE. Ovarian cysts are occasionally pedunculated (growing on the end of stalks). Such cysts may twist on their peduncles and become gangrenous, which is an emergency situation requiring surgery.

Dermoid cysts, also called teratomas or germ cell cysts, are much less common though more troublesome because they can grow quite large. The key characteristic of a dermoid cyst is that it consists primarily of epithelial tissue though may also contain fatty tissue and fragments of HAIR, CARTILAGE, BONE, and sometimes TEETH. Dermoid cysts are congenital (present from birth). Doctors do not know how they occur though believe they arise from cells that escape migration when the three layers of the early EMBRYO (mesoderm, ectoderm, and endoderm) develop.

The doctor detects most ovarian cysts incidentally during routine PELVIC EXAMINATION or ULTRASOUND of the lower abdomen done for other reasons. When a woman does have symptoms they are often nonspecific in nature, such as abdominal bloating or pressure, CONSTIPATION, URINARY INCONTINENCE or URINARY FREQUENCY, or pain during SEXUAL INTERCOURSE (dyspareunia). Abdominal or transvaginal ultrasound or abdominal COMPUTED TOMOGRAPHY (CT) SCAN help the doctor confirm the diagnosis. When these diagnostic imaging procedures are not conclusive, the doctor may perform diagnostic laparoscopy to look at the cyst and take a tissue sample for biopsy.

Most ovarian cysts go away without treatment or intervention. The gynecologist may recommend surgical removal of an ovarian cyst that is large, persistent, or symptomatic (causes discomfort, irregular menstrual periods, or bleeding) or when the cyst has suspicious features that cause the gynecologist to want to rule out OVARIAN CANCER. Though ovarian cysts are not cancerous and very seldom become cancerous, they can co-exist with cancerous tumors. As well, ovarian cancer tumors commonly have cystic characteristics. Often it is possible to remove the cyst without damaging the ovary. When the cyst is large or questionable the surgeon may need to remove the entire ovary (OOPHORECTOMY). As long as the remaining ovary is healthy and functional, removing a single ovary does not affect the menstrual cycle or FERTILITY.

See also OVARIES; SURGERY BENEFIT AND RISK ASSESSMENT.

ovaries The female organs of reproduction, also called the female gonads. The ovaries produce OVA (eggs) and sex hormones, predominantly ESTROGENS and PROGESTERONE as well as small amounts of ANDROGENS. A woman has two ovaries, one ovary on each side of the UTERUS in the lower abdomen. Ligaments suspend the ovaries in place within the abdominal cavity. Each ovary is about the size, shape, and consistency of a large olive. At birth it contains the full complement of ova that will supply a woman for all her years of FERTILITY.

The ovary has two distinct layers of structure, an outer cortex and an inner medulla. The ovarian cortex contains the ovarian follicles, each of which holds an immature ovum (egg), also called a GAMETE or germ cell. The fibrous tissue of the ovarian medulla, made up of stroma cells, contains the ovary's BLOOD vessels, LYMPH vessels, and nerves. The layer of cells covering the ovary is the epithelium; it is made up of epithelial cells (the same type of cell that makes up the SKIN and mucous membranes throughout the body).

Beginning during PUBERTY with the onset of MENSTRUATION, hormonal influences ripen one ovum (sometimes called an oocyte) each MENSTRUAL CYCLE. The ovary releases the ovum into a pocket of fluid that surrounds it. The fimbriae of the fallopian tube (fluted edges of the tube's open end) float in this fluid, extending toward but not touching the ovary. The undulating movements of the fimbriae pull the released ovum into the fallopian tube where, if SPERM are also present, fertilization may occur.

The PITUITARY GLAND releases FOLLICLE-STIMULATING HORMONE (FSH) and LUTEINIZING HORMONE (LH) at different phases of the menstrual cycle to stimulate the sequence of events that will cause the maturation of an ovum. Several ova typically begin the maturation process during each menstrual cycle though usually only one will complete it. The follicle expels the mature, or ripe, ovum. The cells of the follicle produce estrogens and proteins. The developing ovum is a haploid cell—that is, is contains precisely one half the complement of chromosomes (23) necessary to support human

life. When the ovum merges with the sperm, the resulting ZYGOTE contains the full complement of chromosomes (46).

HEALTH CONDITIONS THAT AFFECT THE OVARIES

ENDOMETRIOSIS	OVARIAN CANCER
OVARIAN CYST	POLYCYSTIC OVARY SYNDROME (PCOS)
PREMATURE OVARIAN FAILURE (POF)	TURNER'S SYNDROME

For further discussion of the ovaries within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System." For further discussion of the ovaries within the context of the structures and functions of the endocrine system, please see the overview section "The Endocrine System."

See also CELL STRUCTURE AND FUNCTION; CONCEPTION; CONTRACEPTION; PREGNANCY; TESTICLES.

ovulation The maturation and release of an ovum (egg) during a woman's monthly MENSTRUAL CYCLE. Ovulation establishes FERTILITY (the physiologic ability to conceive a PREGNANCY); only during ovulation may pregnancy occur. Ovulation marks the transition from the proliferative phase to the luteal phase of the menstrual cycle, during which the PITUITARY GLAND's release of LUTEINIZING HORMONE (LH) stimulates the ovarian follicle (sometimes called the graafian follicle) to rupture. The follicle expels the ripened ovum into a small pool of fluid that surrounds the ovary. The fimbriae (fluted edges of the fallopian tube) float in this fluid. As the fimbriae undulate they draw the ovum toward them and into the fallopian tube, where contractions of the tube's wall propel the ovum along the fallopian tube toward the UTERUS. FERTILIZATION, if it is to occur, takes place in the fallopian tube.

It is very difficult to calculate or determine the timing of ovulation. Though ovulation generally occurs within 10 to 15 days after the start of the previous menstrual period, its timing depends on numerous factors, most of which are hormonal. Body temperature rises slightly and the quality of cervical mucous changes during ovulation. Home ovulation testing kits can determine ovulation with fair accuracy; laboratory tests done through the doctor's office are more precise. Ovulation timing is important for women who are trying to conceive, and also for women who are trying to avoid conception. The rhythm method, also called periodic abstinence, relies on avoiding SEXUAL INTERCOURSE during ovulation as a means of CONTRACEPTION.

For further discussion of ovulation within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); CERVIX; FALLOPIAN TUBES; MENSTRUATION; MITTELSCHMERZ; OVARIES.

P–R

Paget's disease of the breast A rare presentation of BREAST CANCER, also called Paget's disease of the nipple. Researchers believe Paget's disease of the BREAST occurs when disordered cells from a cancer within the breast migrate to the SKIN surface, most likely through the milk ducts, to infiltrate the tissues of the outer breast and the nipple. Paget's disease of the breast is most commonly associated with an underlying invasive breast cancer or ductal cancer in situ (DCIS).

The symptoms of Paget's disease of the breast may develop over months to years, and typically begin with a scaly RASH that may itch or burn. The skin of the nipple and the areola (the area around the nipple) may crack and bleed. Because skin conditions such as atopic DERMATITIS (also called eczema) and PSORIASIS commonly affect the breasts, early symptoms are often misdiagnosed as dermatologic. One subtle difference is that Paget's disease of the breast begins in the nipple and spreads to the areola, whereas dermatologic conditions begin in the areola and extend to the nipple. As Paget's disease of the breast advances, the nipple may invert or there may be bloody discharge from the nipple.

The diagnostic path typically includes MAMMOGRAM (X-RAY of the breast) and biopsy of the cells of the nipple and underlying breast tissue. ULTRASOUND of the breast may reveal tumors within the breast. Treatment begins with surgery to remove the cancer, which may be breast-conserving surgery when the cancer remains fairly localized and simple or radical MASTECTOMY when the cancer is widespread within the breast. RADIATION THERAPY, HORMONE THERAPY (such as with tamoxifen) when the underlying cancer is hormone sensitive, and CHEMOTHERAPY are common adjuvant (follow-up) treatments.

See also CANCER TREATMENT OPTIONS AND DECISIONS; PAGET'S DISEASE OF THE BONE.

Pap test A screening test for disorders of the CERVIX, notably CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN) and CERVICAL CANCER. A Pap test, also called a Papanicolaou test, is the laboratory examination of cells swabbed from the cervix during a PELVIC EXAMINATION. The test derives its name from the doctor who developed it. Women over age 18 should have Pap tests every one to three years, depending on their health status. A woman who has had a total HYSTERECTOMY (surgical removal of the UTERUS including the cervix) for reasons other than cancer does not need Pap tests unless she has a history of HUMAN PAPILLOMAVIRUS (HPV). When the hysterectomy was for cancer or was a simple hysterectomy (removal only of the uterus), the woman needs Pap tests according to routine recommendations.

See also COLPOSCOPY.

paraphimosis A condition in which the foreskin retracts onto the shaft of the PENIS and will not return to its normal position to cover the glans (tip of the penis). Paraphimosis can only occur in an uncircumcised man. The foreskin swells and acts as a tourniquet, constricting the flow of BLOOD and causing the shaft of the penis to engorge while cutting off the blood supply to the glans. Paraphimosis requires immediate medical attention to prevent permanent damage, including GANGRENE that necessitates AMPUTATION, to the penis.

Treatment for paraphimosis includes measures to reduce swelling such as ice and compression dressings to the penis. Injection of hyaluronidase, an enzyme, often rapidly reduces the swelling (edema). Once the swelling goes down the doctor may then gently manipulate the foreskin back

PAP TEST RECOMMENDATIONS

Woman's Age	Health Status	Pap Test Interval
under 21	sexually active	every year
21 to 30	all women regardless of health status	every year
31 to 64	three consecutive normal Pap tests no SEXUALLY TRANSMITTED DISEASES (STDS)	every two to three years
31 to 64	multiple sex partners HUMAN PAPILLOMAVIRUS (HPV) INFECTION abnormal Pap test within three years has had treatment for cancer of the CERVIX or endometrium (UTERUS)	every year
65 to 70	normal Pap tests for the previous 10 consecutive years total HYSTERECTOMY	no longer necessary
any age	mother took diethylstilbestrol (DES) when she was pregnant HIV positive organ transplant recipient long-term corticosteroid therapy impaired immune function	every year

over the glans. When these measures are inadequate, the doctor may make an incision through the foreskin to release it. The definitive treatment for paraphimosis is CIRCUMCISION (surgical removal of the foreskin).

See also PHIMOSIS.

pelvic examination A manual and visual examination of a woman's VULVA, VAGINA, and CERVIX. A routine pelvic examination has three parts: visual examination of the external GENITALIA, bimanual palpation, and speculum examination of the inner vagina and the cervix. A pelvic examination is painless and is part of a ROUTINE MEDICAL EXAMINATION for women beginning around age 18 and continuing throughout life. For a routine pelvic examination a woman lies on her back on the examination table with her feet in stirrups and her knees spread apart. The doctor also performs pelvic examination during labor to assess the status of the cervix and progression of labor.

Visual examination The doctor visually examines the external genitalia to detect abnormalities such as growths, sores, discoloration, and other indications of INFECTION or disease.

Bimanual examination For the bimanual portion of the pelvic exam the doctor inserts two gloved and lubricated fingers into the vagina and with the other hand palpates the outside of the abdomen. This procedure allows the doctor to feel the size and placement of the UTERUS and the OVARIES, which may detect abnormalities such as swelling, hypersensitivity or PAIN, displacement (such as tipped uterus), and other indications of health concerns.

Speculum examination The doctor then inserts a lubricated speculum into the vagina. The speculum has two opposing blades that fit together to form a smooth, thin blade that easily enters the vagina. Once the speculum is in position the doctor gently opens the blades to spread apart the walls of the vagina, providing access to the cervix. The doctor visually examines the cervix and inner vagina with the aid of a bright light, and may take a cervical smear (sampling of cells and mucous from the cervix) for a PAP TEST or other laboratory

procedures. The doctor closes the speculum's blade to withdraw the speculum.

See also KEGEL EXERCISES; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

pelvic inflammatory disease (PID) A bacterial INFECTION involving the UTERUS, FALLOPIAN TUBES, CERVIX, and VAGINA. Untreated PID has the potential to become life threatening if it spreads to involve the peritoneal membrane (PERITONITIS), the tissue that encloses the abdominal cavity. Because PID can cause scarring within the fallopian tubes that occludes them (blocks the tubes' openings), chronic or recurrent PID is a leading cause of INFERTILITY in women. PID is a significant health concern in the United States with doctors diagnosing more than one million women with it each year, about half of whom have permanently impaired FERTILITY as a consequence.

The most common cause of PID is recurrent or untreated infection with SEXUALLY TRANSMITTED DISEASES (STDS) such as CHLAMYDIA and GONORRHEA. Other causes include infection that occurs as a postoperative complication after a surgical procedure such as DILATION AND CURETTAGE (D&C) or elective ABORTION. A less common cause of PID is infection resulting from an intrauterine device (IUD), a form of long-term birth control.

Symptoms and Diagnostic Path

It is possible to have PID, especially chronic PID, with few or no symptoms. Many women who have PID typically appear quite ill, however, and may have FEVER and chills in addition to other symptoms. Such symptoms may include

- yellowish or greenish malodorous (foul-smelling) vaginal discharge
- lower abdominal tenderness, cramping, or PAIN
- NAUSEA, VOMITING, and DIARRHEA
- vaginal bleeding between menstrual periods
- irregular or unusually heavy menstrual periods

The diagnostic path includes PELVIC EXAMINATION with vaginal discharge and tissue samples for laboratory analysis and BLOOD tests to evaluate the presence of infection or INFLAMMATION within the body (such as elevated sedimentation rate, white blood cell count, and C-REACTIVE PROTEIN). The cervix and uterus are generally very tender to palpation during the pelvic exam, which is a key diagnostic criterion.

Treatment Options and Outlook

Treatment is prompt administration of ANTIBIOTIC MEDICATIONS, by intravenous (IV) or intramuscular injection for severe symptoms and orally otherwise. Antibiotic therapy may include two or more antibiotic medications, depending on the identified BACTERIA present in the vaginal and cervical cultures. It is essential to take the full course of all antibiotics as prescribed to completely eradicate the infection, which cures the PID. ANALGESIC MEDICATIONS relieve pain and reduce fever to improve comfort. Possible complications of PID include infertility, increased risk for ECTOPIC PREGNANCY, and chronic pelvic pain. The likelihood of these complications increases with each episode of PID, though prompt diagnosis and treatment helps mitigate their risk.

ANTIBIOTICS TO TREAT PELVIC INFLAMMATORY DISEASE (PID)

ampicillin/sulbactam	cefotetan
cefoxitin	ceftriaxone
ciprofloxacin	clindamycin
doxycycline	gentamicin
metronidazole	ofloxacin

Risk Factors and Preventive Measures

The primary risk factor for PID is untreated STD infection. Many people do not have symptoms of STDs yet are infected and pass the infections to their sex partners. Multiple sex partners and unprotected sex are high-risk behaviors for STDs and PID. Measures to prevent infection among sexually active adults include mutual monogamy and latex condom use with every sexual act.

See also HIV/AIDS; MENSTRUATION; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

penis The male organ for URINATION and SEXUAL INTERCOURSE. The penis is an elongated, cylindrical structure made of connective and erectile tissue that extends outside the body from the base of the pelvis. Ligaments attach the root of the penis (segment within the body) to the pubic bone at the

front of the pelvis and the ischial bones at the back of the pelvis. The shaft is the length of the penis that extends outward from the body, and the glans is the end or head of the penis. The URETHRA exits the glans through an opening called the urethral meatus. A loose fold of SKIN, the foreskin (also called the prepuce), covers the glans at birth; beginning around 8 years of age the foreskin retracts from the glans when the penis is erect and returns to drape the glans when the penis is flaccid. CIRCUMCISION is a surgical OPERATION to remove the foreskin.

The interior penis contains three channels: the corpus spongiosum runs along the underside of the penis and houses the urethra; the two corpora cavernosa run side-by-side along the top of the penis and engorge with BLOOD to stiffen and enlarge the penis during ERECTION. A wall of fibrous tissue, the septum, separates and supports the corpora cavernosa. The inside of each corpus cavernosum is a honeycombed network of spaces (called trabeculae) that fill with blood when the penis is erect. The erect penis is capable of penetrating the woman's VAGINA during SEXUAL INTERCOURSE, with sexual stimulation culminating in ORGASM and EJACULATION.

HEALTH CONDITIONS THAT CAN AFFECT THE PENIS

BALANITIS	CANCER OF THE PENIS
CHORDEE	EPISPADIAS
ERECTILE DYSFUNCTION	GENITAL HERPES
HUMAN PAPILLOMAVIRUS (HPV)	HYPOSPADIAS
HYPOGONADISM	KLINEFELTER'S SYNDROME
PARAPHIMOSIS	PEYRONIE'S DISEASE
PHIMOSIS	PRIAPISM

For further discussion of the penis within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also OVARIES; SEXUAL DYSFUNCTION; SEXUAL HEALTH.

perimenopause The period of time during which a woman's body transitions from FERTILITY to MENOPAUSE. The length of perimenopause varies widely though tends to be five to seven years. Perimenopause begins with the changes in the MENSTRUAL CYCLE that herald the approach of menopause. These changes include irregular spacing of menstrual periods (including skipped periods), unusually heavy or light menstrual flow, light breakthrough bleeding (bleeding between periods), and HOT FLASHES.

Bleeding between periods may indicate a health condition that requires treatment. A doctor should evaluate breakthrough bleeding to determine whether it is normal.

Because PREGNANCY is possible during perimenopause, as OVULATION may occur intermittently, a woman who has two consecutive skipped menstrual periods should have a pregnancy test. Women typically experience a range of fluctuating discomforts, notably hot flashes and sleep disturbances, during the menopausal transition. Menopause is a point in time identified in retrospect as the complete absence of menstrual periods for 12 consecutive months.

See also DYSFUNCTIONAL UTERINE BLEEDING (DUB); ENDOMETRIOSIS; MENSTRUATION; UTERINE FIBROIDS.

Peyronie's disease A condition in which a hardened, fibrous plaque forms within the connective tissue of the PENIS, causing a contracture that pulls the penis into a curved position. Researchers do not know what causes the plaque to form. Some believe it represents an autoimmune response (overreaction of the IMMUNE SYSTEM) and others that it occurs as a reaction to traumatic injury. Peyronie's disease generally affects men age 50 and older. The contracture often causes PAIN, particularly when the penis is erect, and interferes with or prevents SEXUAL INTERCOURSE.

The doctor can usually diagnose Peyronie's disease on physical examination of the penis. The plaque is both visible and palpable. The doctor may request an ULTRASOUND of the penis, which shows the extensiveness of the plaque. In about a third of men who have Peyronie's disease the plaque softens and goes away on its own. In other men the curvature progresses to a certain point and then remains stable. It is important to evaluate the potential risks compared to benefits for proposed treatments, which include injecting the plaque with a medication to dissolve the fibrous

tissue and surgery to remove the plaque. A key risk of either procedure is ERECTILE DYSFUNCTION (inability to obtain erections). Generally these treatments are most appropriate when the contracture completely prevents sexual intercourse.

See also CHORDEE; PARAPHIMOSIS; PHIMOSIS; PRIAPISM.

phimosis A condition in which the foreskin becomes fused to the glans of an uncircumcised PENIS and will not retract. Phimosis occasionally occurs as a congenital condition (present at birth) though more often develops later in life, typically as a consequence of poor PERSONAL HYGIENE. Phimosis is the leading cause of BALANITIS, a fungal INFECTION of the inner surface of the foreskin, and can interfere with URINATION and cause PAIN with ERECTION. Recurrent phimosis increases a man's risk for CANCER OF THE PENIS.

The doctor is sometimes able to gently free the adhered foreskin after anesthetizing the penis. Frequent retraction of the foreskin and diligent cleansing are necessary to prevent phimosis from recurring. When this is not effective or phimosis becomes chronic, the recommended treatment is CIRCUMCISION, an OPERATION to surgically remove the foreskin. Though in some men an unusually tight foreskin (congenital phimosis) is the primary cause of phimosis, diligent personal hygiene can prevent most phimosis. It is important for uncircumcised boys and men to clean beneath the foreskin every day by retracting the foreskin, washing the glans gently but thoroughly to remove any accumulated secretions, and allowing the foreskin to return to its natural position.

See also CHORDEE; CONGENITAL DISORDERS; PARAPHIMOSIS; PEYRONIE'S DISEASE.

placenta An organ of PREGNANCY that nourishes and sustains the FETUS. The placenta also secretes a number of hormones that maintain the biochemical environment within the woman's body to support the pregnancy. The placenta develops within the first two weeks after the blastocyst implants into the endometrium of the UTERUS, arising from the outer layer of the blastocyst's cells, the trophoblast. The amniotic sac, which encloses the developing fetus, and the UMBILICAL CORD also arise from the trophoblast.

PLACENTAL HORMONES

activin	chorionic adrenocorticotropin
CHORIONIC GONADOTROPIN	chorionic somatomammotropin
CORTICOTROPIN-RELEASING HORMONE (CRH)	CORTISOL
GONADOTROPIN-RELEASING HORMONE (GNRH)	ESTROGENS
INHIBIN	GROWTH HORMONE–RELEASING HORMONE (GHRH)
PROGESTERONE	placental actinogen
RELAXIN	PROLACTIN
	THYROTROPIN-RELEASING HORMONE (TRH)

The placenta uniquely belongs to both the mother and the fetus. Though the maternal BLOOD circulation delivers NUTRIENTS and oxygen to the fetal blood circulation and carries away fetal wastes, the two circulations do not normally mix with each other. The side of the placenta that faces the fetus is the chorion. Fringelike extensions called the chorionic villi permeate the tissue of the maternal portion of the placenta. Fetal blood circulates through the chorionic villi. Arterioles (tiny arteries) and venules (tiny veins) extend from the myometrium (muscular wall of the uterus) into the spaces between the chorionic villi. The arterioles carry maternal blood into the spaces where it circulates around the chorionic villi. Nutrients, oxygen, and wastes pass across the thin membranes that enclose the chorionic villi.

Problems that can arise with the placenta during pregnancy include

- placenta abruptio (also called placental abruption), in which the placenta partially or completely separates from the uterus; partial separation reduces nutrition to the fetus and complete separation is fatal to the fetus
- placenta accreta, in which the tissues that anchor the placenta to the wall of the uterus penetrate the myometrium too deeply, making it difficult for the placenta to separate after birth
- placenta previa, in which the placenta grows partially or completely across the CERVIX, necessitating CESAREAN SECTION to prevent hemorrhage during labor

After the fetus is born a second round of contractions separate the placenta from the uterine

wall and expel it through the VAGINA. The expelled placenta is the afterbirth.

For further discussion of the placenta within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also AMNIOCENTESIS; AMNIOTIC FLUID; CHILDBIRTH; CHORIONIC VILLI SAMPLING (CVS); CONCEPTION; HORMONE.

polycystic ovary syndrome (PCOS) A condition in which the OVARIES produce excessive ANDROGENS, the male sex hormones, resulting in irregular menstrual cycles and often anovulation (absence of egg maturation and release). A common characteristic of PCOS is the formation of multiple and often numerous cysts within the follicles of the ovaries. PCOS, sometimes called Stein-Leventhal syndrome or hyperandrogenic anovulation, is a common cause of INFERTILITY in women.

Researchers believe INSULIN RESISTANCE, an endocrine disorder in which the cells in the body do not appropriately respond to INSULIN, is a key factor in the development of PCOS though do not know the mechanisms of the relationship between the two conditions. PCOS commonly appears among a constellation of symptoms associated with insulin resistance including OBESITY, HYPERLIPIDEMIA (elevated levels of fatty acids in the BLOOD circulation), ATHEROSCLEROSIS (accumulations of fatty plaques within the walls of the arteries), CORONARY ARTERY DISEASE (CAD), and type 2 DIABETES.

Symptoms and Diagnostic Path

The symptoms of PCOS include

- irregular menstrual cycles
- AMENORRHEA (absence of MENSTRUATION) or frequent skipped menstrual periods
- excessive or male pattern body HAIR (HIRSUTISM)
- male pattern thinning of the hair on the head (ALOPECIA)
- pelvic discomfort or PAIN
- inability to conceive (infertility)
- excessive or persistent ACNE

In addition, many women who have PCOS also have HYPERTENSION (high BLOOD PRESSURE) along with other health conditions in the insulin resistance constellation (notably diabetes, hyperlipidemia, and obesity). Though some women who have PCOS have irregular menstrual cycles from MENARCHE (the onset of menstruation) or fail to start menstruating (primary amenorrhea), many women do not suspect they have PCOS until they are unsuccessful in their attempts to become pregnant.

The diagnostic path begins with a comprehensive medical examination including blood tests to measure HORMONE levels, GLUCOSE tolerance test, and PELVIC EXAMINATION, during which the doctor often can palpate (feel) the enlargement and irregular shape of the ovaries that is typical with multiple cysts. Transvaginal or pelvic ULTRASOUND provides visual representation of the ovaries that can confirm the diagnosis.

Treatment Options and Outlook

Though there is no cure for PCOS, medical treatments to regulate the balance of hormones in the body often can restore normal OVULATION and menstruation. For women who are not trying to become pregnant, the medication of choice is an oral contraceptive (birth control pills). Some oral ANTIDIABETES MEDICATIONS that affect how cells respond to insulin are also effective at improving symptoms.

For women who are trying to become pregnant, FERTILITY medications may stimulate ovulation though the risk for multiple pregnancy becomes significant. Some doctors recommend in vitro fertilization (IVF), a method of ASSISTED REPRODUCTIVE TECHNOLOGY (ART), rather than fertility medications for women who have PCOS and wish to become pregnant because IVF allows control over the number of potential fetuses. During pregnancy women who have PCOS have increased risk for spontaneous ABORTION, GESTATIONAL DIABETES, PREECLAMPSIA, and PREMATURE BIRTH, though diligent PRENATAL CARE keeps these risks to a minimum.

A surgical treatment option is ovarian drilling, a laparoscopic OPERATION in which the surgeon uses electrocautery to burn selected ovarian follicles to destroy the cysts they contain. Ovarian drilling typically restores normal ovulation for a limited time, which reduces symptoms overall. However,

the effectiveness of ovarian drilling eventually diminishes as cysts continue to grow in the remaining ovarian follicles.

Nonmedical approaches such as electrolysis or laser hair removal can improve excessive hair growth. Daily physical exercise improves cell sensitivity to insulin, as does maintaining appropriate body weight. Weight loss of 10 to 15 percent often is enough to restore normal menstrual cycles. Weight management also improves conditions that may co-exist with PCOS such as hypertension and diabetes. Women in whom hormonal balance continues such that amenorrhea persists long term (as may occur in untreated PCOS) have increased risk for ENDOMETRIAL HYPERPLASIA and ENDOMETRIAL CANCER (overgrowth and cancer of the endometrium, the lining of the UTERUS).

Risk Factors and Preventive Measures

The primary risk factor for PCOS appears to be insulin resistance. Lifestyle measures to maintain healthy body weight and regulate the insulin–glucose balance often reduce symptoms of PCOS, though there are no certain measures to prevent PCOS. PCOS does appear to run in families, suggesting a genetic role in its development.

See also CONCEPTION; CONTRACEPTION; EXERCISE AND HEALTH; MENSTRUAL CYCLE; OVA; PREMATURE OVARIAN FAILURE (POF); WEIGHT LOSS AND WEIGHT MANAGEMENT.

preeclampsia A complication of PREGNANCY in which a woman develops significant to severe HYPERTENSION (high BLOOD PRESSURE) and elevated protein in the URINE. Preeclampsia, sometimes called toxemia of pregnancy, is more common in a first pregnancy and in pregnant women who are under age 20 or over age 40 and in women who have DIABETES, kidney disease, or hypertension when they become pregnant. Preeclampsia also seems to run in families, suggesting a GENETIC PREDISPOSITION. For the most part, however, doctors do not know what causes preeclampsia to develop. In about 10 percent of women preeclampsia progresses to ECLAMPSIA, in which seizures occur and which is life-threatening for the woman and the FETUS she carries.

The primary symptoms of preeclampsia are

- HEADACHE
- edema (swelling due to fluid retention)
- NAUSEA and VOMITING
- disturbances of vision (blurred or double vision)
- ringing in the ears or other auditory disturbances

The elevation in blood pressure tends to occur as a surge, most commonly in the second and third trimesters. Most often the doctor detects preeclampsia in its early stages through regular PRENATAL CARE visits and monitoring. Prompt diagnosis and treatment with antihypertensive medications to lower blood pressure can often prevent complications from developing. The doctor may also recommend reduced activity or bedrest to help keep blood pressure down. CHILDBIRTH is the most effective treatment. When preeclampsia is moderate to severe and the pregnancy is 37 weeks or beyond, the doctor may induce labor or perform a CESAREAN SECTION (surgical childbirth). Many women who have preeclampsia are able to go through labor and delivery without additional risk to the fetus or themselves.

See also GESTATIONAL DIABETES.

pregnancy The series of events, extending from CONCEPTION to delivery (CHILDBIRTH), through which a blastocyst (the clump of cells that implants in the endometrium, the lining of the UTERUS) becomes a baby. A full-term pregnancy spans 266 days. However, doctors calculate the estimated date of delivery, commonly called the due date, to be 280 days from the start of the last menstrual period.

Confirming Pregnancy

Though a missed menstrual period is the classic first sign of pregnancy, URINE pregnancy tests are now sensitive enough to detect minuscule amounts of pregnancy-related hormones in the urine only a few days after conception and well before the woman misses a period. Home pregnancy tests are generally as accurate as the tests health-care providers use, though following the directions precisely is important. False results are common because of mistakes such as using a urine sample other than the first of the day (which is

the most concentrated) or not properly timing the duration of the test. Most health-care providers will do a pregnancy BLOOD test at the first prenatal visit to confirm the pregnancy. Pregnancy tests, urine or blood, measure the presence of human chorionic gonadotropin (hCG) or beta hCG.

Early signs of pregnancy a woman may detect include

- tender, swollen breasts
- unexplained nausea and vomiting
- aversions to or cravings for certain foods, including smells and sights of them
- profound tiredness
- sensation of lower abdominal bloating
- increased URINATION
- lightheadedness or dizziness

The health-care provider's examination also detects signs of pregnancy, including changes in the texture (by internal palpation) and appearance of the CERVIX and an enlarged, softened uterus. As pregnancy advances the uterus rises out of the pelvis and into the abdomen (beginning around 12 weeks). As part of the diagnostic process the provider uses terminology to identify how many pregnancies and how many deliveries the woman has had previous to the current pregnancy, designating them with the Latin words *gravida* and *para*. A woman who has been pregnant twice and delivered twice is a gravida 2 para 2, for example, and a woman who is pregnant for the first time is a primigravida nullipara or gravida 1 para 0.

Key Changes During Pregnancy

The woman's body undergoes profound changes during the course of pregnancy. Hundreds of hormones unique to pregnancy initiate and facilitate these changes, the most obvious of which are enlarged breasts and a steadily expanding belly. This biochemical flood is also responsible for the emotional swings that characterize early pregnancy. Nearly every body system modifies its functions in some fashion to support the pregnancy and the developing FETUS.

Uterus and abdomen The woman's uterus, pelvis, and abdominal structures flex and expand to accommodate the fetus as it develops and grows. The uterus, for example, can stretch up to 10 times its normal size during pregnancy. The numerous hormones unique to pregnancy act on connective tissue throughout the woman's body to soften ligaments and muscles, providing the pliability necessary to allow this expansion. This softening also accounts for the MUSCLE and JOINT aches, especially in the hips and knees, common in the last months of pregnancy.

The endometrium (lining of the uterus) remains spongy and vascular to support the PLACENTA. A plug of mucus collects in the cervix, helping block BACTERIA from entering the uterus. The tissues of the VAGINA and VULVA engorge with blood, softening in preparation for childbirth. As the pregnancy approaches term, the cervix softens and thins (effaces). With the contractions of labor the cervix dilates and the vagina expands to allow passage of the fetus.

Breasts Changes in the breasts, notably tenderness and swelling, are often the earliest indications of pregnancy as the breasts respond to the hormones. As pregnancy progresses a woman's breasts greatly enlarge and change in preparation for BREASTFEEDING (lactation) after birth. The mammary glands and ducts (milk glands and ducts) swell and around the seventh month begin producing colostrum, a fatty premilk that conveys important NUTRIENTS and antibodies for basic immunity to the infant.

Cardiovascular A woman's blood volume and cardiac output progressively increase as pregnancy advances. The heart enlarges somewhat, HEART RATE goes up, and blood pressure rises. In very early pregnancy the blood vessels dilate in anticipation of the increased blood volume, sometimes resulting in episodes of lightheadedness or dizziness. Some women also get vascular headaches in response to the changes taking place within the muscular walls of the arteries.

Gastrointestinal One of pregnancy's early hallmarks is MORNING SICKNESS, nausea and vomiting doctors believe results from the hormones that surge into the woman's blood circulation when the blastocyst implants. These same hormones are responsible for softening connective tissue and have similar actions on the muscular tissues of the gastrointestinal system, sometimes slowing peristalsis (movement of the intestines) enough to

cause CONSTIPATION. Drinking plenty of fluids, eating foods high in fiber, and walking for at least 30 minutes every day help keep the gastrointestinal system functioning at its best.

In the later months of pregnancy the enlarged uterus displaces the organs of the upper abdomen further upward against the DIAPHRAGM, pressuring the stomach to cause DYSPEPSIA (upset stomach and heartburn) and gastric reflux. These discomforts go away after the baby is born and the abdominal organs return to their normal positions.

Weight gain Weight gain is both normal and essential to support the pregnancy. Appropriate weight gain for a woman who is of healthy weight at the onset of pregnancy is 25 to 35 pounds; in OBESITY less weight gain, 15 to 25 pounds, is healthier for both mother and baby. About 15 to 18 pounds of the weight comes from the baby and organs that support it (uterus, placenta, AMNIOTIC FLUID). The changes in the breasts add 2 to 3 pounds; additional fluids (such as blood) and increased body fat account for the remainder. The most rapid weight gain typically occurs in the second trimester, 2 to 4 pounds per month.

Most women require only an additional 200 to 300 calories a day to meet their increased energy needs. Nutritious EATING HABITS are especially important to meet nutritional needs for vitamins and minerals. Pregnant women should take prenatal vitamins to make sure they receive adequate amounts of vital nutrients. Folic acid (folate) is particularly crucial for proper development of the BRAIN and SPINAL CORD. Supplemental iron boosts the ability of the woman's blood to carry oxygen, helping prevent ANEMIA.

Health Care During Pregnancy

Though pregnancy is a natural event, not a medical condition, routine PRENATAL CARE provides optimal circumstances for the health of the woman and of the fetus. Current medical knowledge and technology make possible high-risk pregnancies as well as early intervention to avert or manage medical complications that may arise in the woman or the fetus. Screening tests and procedures can detect congenital and genetic abnormalities (BIRTH DEFECTS) that may require special medical attention during or after birth.

For further discussion of pregnancy within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also ABORTION; ADOPTION; ECTOPIC PREGNANCY; FAMILY PLANNING; FERTILITY; GESTATIONAL SURROGACY; OVA; PREMATURE BIRTH; STILLBIRTH; ZYGOTE.

premature ovarian failure (POF) A health condition in which a woman's OVARIES stop functioning before age 40. POF is a leading cause of INFERTILITY in women. Though POF causes MENOPAUSE-like symptoms and people (including doctors) sometimes refer to it as premature menopause, women

THE WOMAN'S BODY THROUGH PREGNANCY

Gestational Week	Body Characteristics
4 to 6	UTERUS soft and enlarged; breasts tender and swollen
12	belly begins to bulge; 2 to 4 pounds weight gain
16	darkened nipples and areola; dark line down center of abdomen
20	top of uterus at the level of the belly button; pregnancy obvious; breasts enlarged
24	Braxton-Hicks contractions; top of uterus above belly button; VULVA enlarged due to blood engorgement
28	weight gain of about 1 pound a week; minor swelling of the ankles and feet; size of uterus pressures BLADDER and DIAPHRAGM
32	breasts begin to leak colostrum; fetal movements visible through the abdominal wall
36	top of uterus near the bottom of the sternum; CERVIX begins to soften and thin (efface); pelvic ligaments and muscles soften and stretch
40	Strong Braxton-Hicks contractions; uterus completely fills the abdominal cavity; cervix continues to efface and begins to dilate; breasts engorged and frequently leak colostrum; mucous plug dislodges from cervix; water breaks (amniotic membrane ruptures)

who have POF often have irregular menstrual cycles for years after the onset of POF symptoms and do retain the ability to conceive, whereas menstrual cycles completely cease with menopause, ending the potential for pregnancy.

The reasons for POF are unclear though likely are a mix of genetic, hormonal, and perhaps autoimmune factors. Women who have POF have lower than normal levels of ESTROGENS and higher than normal FOLLICLE-STIMULATING HORMONE (FSH) levels in the BLOOD circulation, suggesting depletion or dysfunction of the ovarian follicles. Doctors do not know whether the abnormal HORMONE levels cause or result from follicular factors. CHROMOSOMAL DISORDERS such as TURNER'S SYNDROME and GENETIC DISORDERS such as ACHONDROPLASIA (a form of SKELETAL DYSPLASIA, often called dwarfism) also are associated with POF.

Symptoms and Diagnostic Path

The symptoms of POF are similar to those of menopause and commonly include

- HOT FLASHES and night sweats
- vaginal dryness and irritation (nonbacterial VAGINITIS)
- painful SEXUAL INTERCOURSE (dyspareunia)
- diminished LIBIDO
- low energy or fatigue
- irritability and mood swings
- irregular menstrual periods

The diagnostic path begins with a comprehensive medical examination, including PELVIC EXAMINATION, and blood tests to measure blood hormone levels (usually including a PREGNANCY test). The doctor may desire genetic tests as well, such as a KARYOTYPE, to evaluate the possibility of a genetic or chromosomal disorder. Women who have very mild Turner's syndrome may first learn of this diagnosis during evaluation for POF, as other symptoms of the syndrome may be so nominal as to escape detection.

Treatment Options and Outlook

Treatment with estrogen and progestin supplementation until closer to the age for natural menopause may relieve many POF symptoms though does not usually improve FERTILITY. However, pregnancy remains possible and is something a woman should consider when her menstrual period does not occur as expected when she is taking hormone supplementation.

Women who have POF have increased risk for OSTEOPOROSIS and CARDIOVASCULAR DISEASE (CVD), and should follow lifestyle practices to support BONE and cardiovascular health. Such practices include calcium supplementation, daily physical exercise such as walking or running for cardiovascular health, resistance activities such as lifting weights to maintain MUSCLE mass and BONE DENSITY, nutritious EATING HABITS, and weight management. ASSISTED REPRODUCTIVE TECHNOLOGY (ART) methods using donor OVA (eggs) may provide pregnancy for a woman who has POF and desires to conceive.

Risk Factors and Preventive Measures

Known risk factors for POF are chromosomal or genetic disorders affecting the sex chromosomes or features of sexual development and ADDISON'S DISEASE (an autoimmune disorder affecting the ADRENAL GLANDS). Medical treatments such as CHEMOTHERAPY and RADIATION THERAPY may cause secondary POF. There are no known measures to prevent POF.

See also AUTOIMMUNE DISORDERS; POLYCYSTIC OVARY SYNDROME (PCOS); SEX CHROMOSOME; WEIGHT LOSS AND WEIGHT MANAGEMENT.

premature birth The delivery of an infant before 37 weeks gestational age, also called preterm birth. Though viability is possible after 24 weeks, many fetal organ systems do not reach maturity sufficient for independent life until near full term. Sometimes there are warning signs of premature birth that allow the doctor to attempt to delay CHILDBIRTH by administering medications to stop uterine contractions. The doctor may also help the FETUS prepare for independent life. Giving the mother injections of betamethasone, a corticosteroid, accelerates the fetus's lung development.

Though premature birth does not present any unusual risk for the woman, it often results in mild to moderate health challenges for the infant. Very early premature birth, between 24 and 32 weeks, presents grave health risks for the infant, who commonly requires extensive medical care

for several weeks to several months, depending on the gestational age at birth. About 10 percent of babies in the United States are born prematurely. The most common causes of premature birth are multiple PREGNANCY and PREECLAMPSIA. Women who have DIABETES, HYPERTENSION (high BLOOD PRESSURE), and chronic kidney disease have increased risk for premature delivery.

See also ABORTION; NEONATAL JAUNDICE; STILLBIRTH.

premenstrual syndrome (PMS) A constellation of symptoms that occurs in a regular pattern aligned with a woman's MENSTRUAL CYCLE. Doctors believe PMS results from the hormonal shift in the balance between ESTROGENS and PROGESTERONE that follows involution of the corpus luteum. This shift sets in motion the events that produce MENSTRUATION. PMS tends to begin during the last half of the luteal phase and continue to the onset of menstrual bleeding, typically spanning five to seven days. As many as 85 percent of women experience some symptoms of PMS; about 10 percent experience symptoms significant enough to interfere with daily activities. Some doctors call debilitating symptoms premenstrual dysphoric disorder (PMDD).

Symptoms and Diagnostic Path

The symptoms of PMS may vary from month to month in a woman and also vary widely among women. Common PMS symptoms include

- irritability, extreme emotions, and mood swings
- MASTALGIA (painful breasts)
- confusion, forgetfulness, and difficulty concentrating
- abdominal cramping and bloating
- low back ache or PAIN
- fluid retention and swelling of the hands, ankles, and feet
- weight gain (as much as two to four pounds)

The diagnostic path begins with a comprehensive medical examination, including PELVIC EXAMINATION. The doctor may ask the woman to keep a daily diary of her symptoms over three to six months, which helps to establish a clear pattern of symptoms and their severity. The doctor may request BLOOD tests and abdominal ULTRASOUND to rule out hormonal imbalances, ovarian conditions, and other possible causes for symptoms.

Treatment Options and Outlook

Mild to moderate PMS often improves with lifestyle modifications, including sufficient sleep, nutritious EATING HABITS, daily physical exercise, MEDITATION or other relaxation methods, and reduced CAFFEINE consumption (though some women find the diuretic and mild stimulant effects of caffeine helpful). BIOFEEDBACK and ACUPUNCTURE are also often effective. Supplementation with B vitamins, vitamin E, and calcium appear to reduce PMS symptoms, though it may take several months for the effect to become apparent. Evening primrose oil, SOY and other PHYTOESTROGENS, DONG QUAI, and BLACK COHOSH are among the herbal remedies that may relieve PMS symptoms. Over-the-counter (OTC) NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) relieve HEADACHE and mastitis, and may reduce other symptoms because of their actions to suppress the release of PROSTAGLANDINS (chemicals that increase the sensitivity of nerves to pain signals).

Selective serotonin reuptake inhibitors (SSRIs), a class of ANTIDEPRESSANT MEDICATIONS, are effective in relieving moderate to severe PMS symptoms and are the current standard of care for PMS as well as PMDD. Researchers believe SSRIs work so well because they influence the neurohormonal interactions that take place in the BRAIN. Though some women find their symptoms improve with oral contraceptives (birth control pills), recent research suggests progesterone (which appears in the synthetic form progestin in many oral contraceptive formulas) is a key factor in causing PMS. Current clinical guidelines recommend oral contraceptives as treatment for PMS only when the woman also desires to take them as a means of preventing PREGNANCY.

Risk Factors and Preventive Measures

PMS occurs only in menstruating women. However, though PMS is very common not all menstruating women experience it. Some research suggests that women may metabolize progesterone differently, accounting for differences in its effects during the menstrual cycle. Lifestyle meas-

ures, medications, or a combination of approaches can help mitigate symptoms for many women, though there are no methods for preventing PMS.

See also DYSMENORRHEA; MEDICINAL HERBS AND BOTANICALS; MENOPAUSE.

prenatal care Routine and preventive health care provided during PREGNANCY to safeguard the health and well-being of the woman and the FETUS. In the United States routine prenatal care consists of regular visits to the health-care provider (family practitioner, obstetrician, or nurse midwife), URINE and BLOOD tests, BLOOD PRESSURE checks, and additional diagnostic procedures as needed such as ULTRASOUND, AMNIOCENTESIS, or CHORIONIC VILLI SAMPLING (CVS). The schedule of visits varies according to the trimester of pregnancy and any specific concerns about the pregnancy.

Ideally, prenatal care begins before CONCEPTION with a focus on nutritious EATING HABITS, healthy weight, appropriate management of any health conditions (such as DIABETES, HYPERTHYROIDISM, and HYPERTENSION), and abstinence from cigarette smoking, ALCOHOL consumption, and substance abuse. The prospective father should share this focus, as the health of both parents contributes to FERTILITY and fetal health. Also ideally, a woman who is planning pregnancy already receives routine medical examinations, including PELVIC EXAMINATION and PAP TEST, according to the recommendations appropriate for her age, sexual activity, and health history. Lifestyle habits to maintain the health of the woman and the fetus remain significant for the duration of pregnancy.

Health experts strongly encourage all women of childbearing age, regardless of their intentions toward pregnancy, to take a folic acid supplement. Folic acid, also called folate, significantly reduces the risk for serious BIRTH DEFECTS called NEURAL TUBE DEFECTS. However, the neural tube (the rudimentary CENTRAL NERVOUS SYSTEM) develops very early, well before a woman suspects she might be pregnant. Taking 400 micrograms (mcg) of folic acid supplement daily provides protection even when pregnancy is unexpected (as is the case with half of pregnancies that occur in the United States) and provides nutritional benefit for the woman. Oral contraceptives (birth control pills) deplete folic acid.

Prenatal Care: First Trimester

Routine prenatal care visits occur monthly during the first trimester, which extends through the 12th week of pregnancy. The first prenatal visit is more extensive than subsequent visits because the health-care provider conducts a comprehensive medical examination, including pelvic exam, and collects detailed information about the woman's health history, including any previous pregnancies, SEXUALLY TRANSMITTED DISEASES (STDS), childhood diseases, and immunizations. At the first prenatal visit the health-care provider also establishes a baseline of vital data such as height, weight, blood pressure, and size of the pelvic opening and the UTERUS. Routine blood tests done on the first prenatal visit commonly check BLOOD TYPE including Rh factor, ANEMIA, and antibodies for MUMPS, MEASLES, CHICKENPOX, HEPATITIS B, RUBELLA, and SYPHILIS. The provider may also recommend a blood test for HIV/AIDS and screening of both parents for cystic fibrosis if not yet done.

Another priority on the first prenatal visit is estimation of the anticipated due date for birth, which is important to assess whether the pregnancy and fetal growth are progressing as they should. Adding seven days and subtracting three months from the date the last menstrual period started gives the approximate due date, which the provider compares to findings from the pelvic examination to assess the age of the fetus.

At each subsequent prenatal visit during the first trimester the health-care provider tests a urine sample for GLUCOSE and protein, obtains weight and blood pressure, and measures the growth of the uterus. Pelvic exams are not usually necessary. If there are concerns about GENETIC DISORDERS or CHROMOSOMAL DISORDERS the provider may offer CVS (chorionic villi sampling) between the 10th and 12th weeks. At the last visit of the first trimester the health-care provider is often able to detect the fetal heartbeat using Doppler ultrasound.

Prenatal Care: Second Trimester

Routine prenatal visits continue monthly during the second trimester, the 13th through the 26th weeks of pregnancy. The growth of the uterus is more apparent and measurements of it more precise, allowing the health-care provider to refine

the prospective due date. Weight, blood pressure, and urine sample for glucose and protein remain staples of prenatal visits in the second trimester.

Around the 18th week the health-care provider offers a set of screening blood tests, the triple screen or the quad screen. These tests measure certain hormones and proteins in the woman's blood that may suggest neural tube defects such as SPINA BIFIDA and chromosomal disorders such as DOWN SYNDROME. The results of these tests are specific to the gestational age so the provider will be as certain as possible about the due date before conducting them.

It is important for the woman, her partner, and the provider to discuss the implications of positive results from screening tests, and for the woman and her partner to consider what actions they might take. The provider typically recommends amniocentesis to further evaluate positive triple screen or quad screen results. The provider may recommend abdominal ultrasound around the 20th week if the due date is questionable or if there is reason to suspect abnormalities in fetal development. At the end of the second trimester the provider typically requests a glucose challenge test to check for GESTATIONAL DIABETES as well as blood tests to check for anemia.

MATERNAL SCREENING BLOOD TESTS

Triple Screen
ALPHA FETOPROTEIN (AFP)
beta human chorionic gonadotropin (beta-HCG)
unconjugated estriol (uE3)
Quad Screen
AFP
beta-HCG
uE3
pregnancy-associated plasma protein A (PAPP-A)

Prenatal Care: Third Trimester

Routine prenatal care visits shift to every two weeks between 28 and 36 weeks and weekly from 36 weeks until delivery. The health-care provider continues to check weight, urine, and blood pressure. Early in the third trimester the provider discusses the potential for delivery by CESAREAN SECTION if the fetus is in a breech position or there are other circumstances that might increase the risk to the fetus or the woman with a vaginal delivery.

At the 34th or 35th week the provider cultures swabbed samples from the VAGINA and rectum for group B streptococcus (GBS) BACTERIA, which some women harbor without harm to themselves but that can cause life-threatening INFECTION in the newborn. Women who test positive for GBS receive ANTIBIOTIC MEDICATIONS when they go into labor. The provider also monitors the status of GENITAL HERPES, when this STD is present, to be prepared for cesarean section should an outbreak occur near the anticipated time of delivery.

See also CONGENITAL ANOMALY; FAMILY PLANNING; FETAL ALCOHOL SYNDROME; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

priapism A condition in which a man's PENIS remains erect for longer than four hours. Priapism is involuntary (not a function of sexual stimulation), painful, and requires immediate medical attention to prevent permanent damage to the penis and preserve sexual function. Priapism is most often a SIDE EFFECT of medication, notably medications to treat ERECTILE DYSFUNCTION and the antidepressant medication trazodone. It also may occur as a complication of SICKLE CELL DISEASE, GENITAL TRAUMA, and PROSTATE CANCER. Treatment may include evacuation of BLOOD from the corpora cavernosa, the tubular channels within the penis that fill with blood to establish an erection, via needle and syringe or intravenous catheter. The doctor may also inject the penis with vasoconstrictor medications. If medical interventions fail, surgery may be necessary to implant a shunt that allows blood to drain from the penis.

See also ANTIDEPRESSANT MEDICATIONS; PARAPHIMOSIS; PEYRONIE'S DISEASE.

prostate cancer A malignant (cancerous) tumor that arises from the glandular tissue of the PROSTATE GLAND, a walnut-size structure that encircles a man's URETHRA at the base of the BLADDER. Prostate cancer is one of the HORMONE-DRIVEN CANCERS that appears to have some genetic foundations as it tends to run in families. Prostate cancer also strongly correlates to increased age; it is rare among men under age 50 and affects more than half of men over age 70.

Prostate cancer is the most frequently diagnosed cancer among men in the United States and is primarily found in men over age 60. Though prostate cancer may take an aggressive path with widespread METASTASIS that leads to premature death, prostate cancer more often than not is a slow-growing cancer and runs a course that doctors can control through various treatments. Far more men die *with* prostate cancer than *from* prostate cancer. With early detection and treatment, prostate cancer may be curable.

The symptoms of prostate cancer are often difficult to distinguish from the symptoms of noncancerous conditions that affect the prostate gland, particularly BENIGN PROSTATIC HYPERPLASIA (BPH). All men eventually develop some degree of BPH as they grow older, enlargement of the prostate gland begins to occur as a natural dimension of aging. However, BPH is not and does not become prostate cancer, though a man may have both conditions concurrently.

Symptoms and Diagnostic Path

Early to moderately advanced prostate cancer may cause no symptoms, with diagnosis resulting from further investigation of an abnormally high PROSTATE-SPECIFIC ANTIGEN (PSA) BLOOD level or abnormal findings during DIGITAL RECTAL EXAMINATION (DRE) performed during a ROUTINE MEDICAL EXAMINATION. When symptoms are present they may include

- frequent URINATION, particularly at night (NOCTURIA)
- incomplete emptying of the bladder with urination, sometimes resulting in URINARY URGENCY, URINARY FREQUENCY, and URINARY TRACT INFECTION (UTI)
- reduced urinary flow, urinary hesitation (difficulty starting the flow of urine), and dribbling (difficulty stopping the flow of URINE)
- blood in the urine (HEMATURIA) or SEMEN (hematospermia)
- sensation of heaviness or fullness in the lower abdomen (pelvic area)
- low BACK PAIN or rectal pressure

The diagnostic path may include DRE to palpate the prostate gland, blood tests to measure PSA levels and detect the presence of other TUMOR MARKERS, urinalysis, transrectal ULTRASOUND (TRUS), and biopsy (multiple tissue samples) of the prostate gland.

STAGING AND GRADING OF CANCER are critical for identifying and selecting the most appropriate treatment options. Several systems exist for cancer staging and grading. Because prostate cancer cells typically invade different areas of the prostate gland at varying levels of what pathologists call architectural disorder—the extent to which the cell structure deviates from normal—conventional staging and grading methods often cannot accurately classify the prostate cancer overall. Some areas of invasion may be fairly advanced and others minimally involved. The Gleason system and the Jewett system are methods unique to prostate cancer and the ones most doctors use to guide treatment decisions. In addition, conventional staging methods provide further classification.

Gleason pattern and score The Gleason system allows the pathologist to select the pattern (sometimes called grade) of the two most predominant architectures (primary and secondary) among the biopsy samples and combine them into a score that represents the character of the prostate cancer overall. There are five patterns and nine scores possible within the Gleason system. The lower the Gleason score (also called the Gleason sum), the more likely the cancer is confined and will respond to treatment. However, the patterns that establish the score are also important. For example, a prostate cancer that has a Gleason score of 7 coming from 3 + 4 has a more positive prognosis than one with a Gleason score of 7 coming from a 4 + 3 because the first number indicates the primary pattern and pattern 3 is less aggressive than pattern 4. It is important to know both patterns as well as the score.

Jewett staging system The Jewett system, also called the Jewett-Whitmore system, assigns four alphabetic values to the extent of cancer metastasis, with numeric subvalues for more precise classification.

Conventional staging Some doctors additionally use conventional staging and grading systems

GLEASON PATTERNS AND SCORES FOR PROSTATE CANCER

Gleason Pattern	
pattern 1	cells and architecture nearly normal (well differentiated)
pattern 2	cells nearly normal though glandular cells beginning to invade MUSCLE tissue within the PROSTATE GLAND
pattern 3	cells still maintain glandular structure though invasion of muscle tissue within the prostate gland is significant; possible regional METASTASIS
pattern 4	significant cell abnormality with loss of normal architecture and distorted glandular structure; probable regional metastasis; possible distant metastasis
pattern 5	cells and architecture completely irregular and abnormal (undifferentiated); probable distant and multiple metastases

Gleason Score	
2	lowest possible score; very early cancer with excellent prognosis
3 to 4	slow growing tumor; early cancer with good prognosis
5 to 6	mildly aggressive tumor likely confined to the prostate gland
7	moderately aggressive tumor with possible regional metastasis
8 to 9	aggressive tumor with regional metastasis
10	highly aggressive tumor with multiple distant metastases

JEWETT STAGING SYSTEM CLASSIFICATIONS

stage A	very early, localized cancer; only indication is elevated BLOOD PROSTATE-SPECIFIC ANTIGEN (PSA) level
	A1: well-differentiated or single site within PROSTATE GLAND
	A2: clearly abnormal cells or multiple sites within prostate gland
stage B	localized cancer palpable via DIGITAL RECTAL EXAMINATION (DRE); may cause mild symptoms
	B1: single site
	B2: multiple sites
stage C	METASTASIS to adjacent tissue but not to LYMPH nodes
	C1: tumor is outside the prostate gland but nonobstructive
	C2: tumor obstructs the BLADDER or the URETHRA (urinary symptoms)
stage D	metastasis to lymph nodes or distant organs
	D1: regional LYMPH NODE involvement
	D2: distant lymph node or organ involvement (including BONE)
	D3: RECURRENCE after treatment

to further classify and understand the prostate cancer's characteristics to optimally tailor treatment approaches. The two main conventional staging systems are

- the numeric system, which identifies five levels of tumor aggressiveness (stage 0 through stage 4, or IV)
- the American Joint Committee on Cancer (AJCC) tumor, node, and metastasis (TNM) system, which assigns numeric values to the size of the tumor, invasion of LYMPH nodes, and spread to distant organs or structures

Treatment Options and Outlook

The treatment of choice for men under age 70 is nearly always PROSTATECTOMY, a surgical OPERATION to remove the prostate gland, with adjuvant (follow-up) CHEMOTHERAPY, RADIATION THERAPY, or HORMONE THERAPY as appropriate. Radiation therapy is most effective when the cancer remains confined to the prostate gland. For men over age 70, in

whom prostate cancer is likely to be slow growing and remain localized, the doctor may recommend less invasive approaches such as diligent monitoring (watchful waiting) or radiation therapy (external beam or internal seeding).

No matter his age at the time of diagnosis, a man must consider the many factors that contribute to the relative benefits and risks of treatment options for his stage and grade of cancer, prognosis, other health conditions, and personal desires. Treatments such as surgery and hormone therapy may affect sexual function and have other undesirable side effects. It is important to fully understand the potential implications of treatment options and their effects on QUALITY OF LIFE. Though prostate cancer is the second-leading cause of cancer deaths among men in the United States (LUNG CANCER being first), treatment provides long-term management and prostate cancer is not fatal in the majority of men who develop it.

Risk Factors and Preventive Measures

The most significant risk for prostate cancer is age. Prostate cancer is uncommon in men under age 50 though is present in about half of men over age 80. Other factors that increase the risk for prostate cancer are African American heritage and long-term EATING HABITS that feature foods high in saturated fat. There is some evidence that dietary consumption of SOY proteins, such as in soybean-based foods and in nutritional supplement products, and LYCOPENE, found in tomatoes and pink grapefruit, improve the ability of prostate glandular cells to resist cancerous changes. The medicinal botanical product SAW PALMETTO, available in the United States as a nutritional supplement, may help maintain overall PROSTATE HEALTH.

Health experts differ in their opinions about the value of routine screening procedures, such as DRE and PSA blood levels, for detecting prostate cancer and especially for improving the outcome of treatment. PSA in particular tends to generate a high percentage of false-positive findings, thrusting men into more invasive diagnostic procedures that have increased risks as well as heightened emotional stress. However, both DRE and PSA are components of a routine medical examination in the United States for men over age 50. It is important for a man and his doctor to carefully and comprehensively evaluate all aspects of the man's personal prostate health and to weigh the risks and benefits of further diagnostic assessment.

See also CANCER TREATMENT OPTIONS AND DECISIONS; CARCINOMA; DIET AND HEALTH; LIFESTYLE AND HEALTH; MEDICINAL HERBS AND BOTANICALS; SURGERY BENEFIT AND RISK ASSESSMENT.

prostate gland The gland in the male reproductive tract that produces most of the volume of SEMEN. About the shape and size of a walnut, the prostate gland wraps around the URETHRA at the neck of the BLADDER. The back of the prostate gland rests against the front wall of the RECTUM. A tough, fibrous membrane forms a single capsule enclosing the 30 to 50 clusters of glandular tissue that make up the prostate gland. There are three distinct structures of glandular tissue, which urologists refer to as zones—peripheral, transition, and central—though how the zones differ in function remains unknown. The prostate gland also contains nonglandular cells, primarily MUSCLE and connective tissue cells that help move prostatic secretions into the urethra.

Prostate gland cells produce their secretions under stimulation by TESTOSTERONE, which reaches them through the BLOOD circulation. The seminal vesicles, which lie just behind the prostate gland, store mature SPERM encased in a thick, jellylike solution that prevents them from motility. During ORGASM and EJACULATION, the seminal vesicles and the prostate gland each contract, mixing sperm and prostatic fluid in the urethra to form semen. The prostatic fluid contains an enzyme, PROSTATE-SPECIFIC ANTIGEN (PSA), that thins the semen to allow the sperm to become motile. Ejaculation then carries the semen through the urethra and out the tip of the PENIS.

As a man ages the prostate gland slowly enlarges, a condition called BENIGN PROSTATIC HYPERPLASIA (BPH). In most men BPH remains innocuous, causing no symptoms or even awareness of its presence. Other health conditions that can affect the prostate gland are PROSTATITIS (INFLAMMATION or INFECTION) and PROSTATE CANCER. The surgical OPERATION to remove the prostate gland is

PROSTATECTOMY. The doctor can palpate (feel) the prostate gland through the wall of the rectum during DIGITAL RECTAL EXAMINATION (DRE), which helps detect prostate enlargement as well as abnormalities that suggest other health concerns affecting the prostate gland. Because the risk for prostate cancer increases after age 40, DRE palpation of the prostate gland becomes part of the ROUTINE MEDICAL EXAMINATION for men age 40 and older.

HEALTH CONDITIONS THAT CAN AFFECT THE PROSTATE GLAND

bacterial PROSTATITIS	BENIGN PROSTATIC HYPERPLASIA (BPH)
nonbacterial prostatitis	prostadynia
PROSTATE CANCER	prostatic ABSCESS

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CANCER PREVENTION.

prostate health Measures a man can take throughout his life to maintain healthy function of his PROSTATE GLAND. The prostate gland, which wraps around the URETHRA at the base of the BLADDER, produces the primary volume of SEMEN, the fluid that carries SPERM out of the body during EJACULATION, and the enzyme PROSTATE-SPECIFIC ANTIGEN (PSA), which thins the semen to permit sperm motility. The prostate gland functions unobtrusively through most of a man's life. In early to mid-adulthood the most significant risk to prostate health is INFECTION (PROSTATITIS), which may be due to the spread of a sexually transmitted disease (STD) such as GONORRHEA or may result from non-STD causes.

In late midlife and beyond the prostate gland begins to slowly enlarge, a natural aspect of aging. Doctors call the enlargement BENIGN PROSTATIC HYPERPLASIA (BPH). For about half of men over age 60 BPH becomes significant enough to constrict or obstruct the urethra (the tubelike structure that drains URINE from the bladder), causing symptoms of urinary obstruction such as URINARY FREQUENCY and hesitation. With increasing age the risk for PROSTATE CANCER, the most serious health condition affecting the prostate gland, also increases.

Dietary and lifestyle measures may slow the progression of both BPH and prostate cancer. Foods that support prostate health include

- SOY (soybeans, soy protein, tofu, tempeh)
- tomatoes and tomato-based foods such as tomato sauce and tomato paste, which contain LYCOPENE
- pink grapefruit and watermelon, which also contain lycopene
- cruciferous vegetables (broccoli, cauliflower, cabbage, kale), which contain sulforaphane and other isothiocyanates, substances that appear to help prostate gland cells fight cancer

A number of studies show the herbal remedy SAW PALMETTO can improve the symptoms of mild to moderate BPH, apparently by shrinking the prostate gland tissues. Some studies show a correlation between high BODY MASS INDEX (BMI) and more aggressive prostate cancers, and other studies demonstrate a lower risk for cancer overall (as well as CARDIOVASCULAR DISEASE and DIABETES) with healthy body weight and regular physical exercise. In the United States, preventive health-care recommendations call for PSA BLOOD level measurements and DIGITAL RECTAL EXAMINATION (DRE) as part of a man's ROUTINE MEDICAL EXAMINATION beginning around age 50. These tests may detect abnormal function or size of the prostate gland that could be early indications of BPH or prostate cancer.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CANCER PREVENTION; DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND HEALTH; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS; SEXUAL HEALTH; URETHRITIS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

prostatectomy A surgical OPERATION to remove part or all of the PROSTATE GLAND. The prostate gland encircles the URETHRA at the base of the BLADDER. It produces the fluid that mixes with SPERM to form SEMEN and produces the enzyme PROSTATE-SPECIFIC ANTIGEN (PSA), which facilitates sperm motility after EJACULATION. Prostatectomy is primarily treatment for PROSTATE CANCER and BENIGN PROSTATIC HYPERPLASIA (BPH) that constricts the urethra to the extent that it interferes with URINATION. Removal of the prostate gland ends a man's FERTILITY though not necessarily his ability to have and ERECTION and ORGASM.

Surgical Procedure

Surgeons may choose from a number of operations to remove the prostate gland. The choice depends on the reason for the operation, the size of the prostate gland, and the man's overall health status. There are six commonly performed prostatectomy operations: transurethral retrograde prostatectomy (TURP), transurethral incision of the prostate (TUIP), three open prostatectomy operations (suprapubic, retropubic, and perineal), and radical open prostatectomy.

Transurethral retrograde prostatectomy (TURP) TURP has long been the standard, and remains the most common, surgical operation to remove obstructive prostate gland tissue due to BPH (noncancerous prostate gland enlargement) when the prostate gland remains relatively small. The surgeon uses an endoscopic instrument called a resecting cystoscope or resectoscope, inserted through the PENIS and urethra to the prostate gland.

The surgeon passes a cutting tool through the resectoscope to make an incision through the urethra and remove part or all of the prostate gland by shaving away layers of tissue. After removing the prostate gland the surgeon sutures the urethra back to the neck of the bladder. The removed shreds of tissue collect in the bladder and pass out with the URINE over the first few days after surgery. TURP generally requires three days in the hospital and two to four weeks recovery time until full return to normal activities. A man who has had a TURP usually retains erectile function though has RETROGRADE EJACULATION (ejaculation into the bladder).

Transurethral incision of the prostate (TUIP) TUIP is a cystoscopic procedure in which the surgeon makes a series of small incisions through the urethra into the prostate gland. The incisions relieve the pressure the enlarged prostate gland is exerting against the urethra, without removing prostate tissue, restoring the free flow of urine. TUIP is treatment only for noncancerous prostate enlargement, such as BPH, and is used only in limited circumstances that depend on the size and structure of the prostate gland. TUIP is often an AMBULATORY SURGERY procedure (a same-day surgery) with full return to normal activities in three to five days. Erectile and ejaculatory functions nearly always remain normal.

Open prostatectomy The three operations of open prostatectomy, sometimes called simple prostatectomy, involve making an incision through the surface of the SKIN to reach the prostate gland. The incision for suprapubic or retropubic prostatectomy extends from the navel (belly button). In the suprapubic approach the surgeon reaches the prostate gland through the bladder. In the retropubic approach the surgeon reaches the prostate gland without entering the bladder. The incision for perineal prostatectomy is between the SCROTUM and the ANUS. Open prostatectomy removes the prostate gland and seminal vesicles intact. The surgeon may also remove nearby LYMPH nodes (lymphadenectomy) when the operation is to treat prostate cancer.

Open prostatectomy is major surgery that requires a stay of up to eight days in the hospital and six to eight weeks recovery (sometimes longer) before return to regular daily activities. There is moderate risk for significant complications such as bleeding, URINARY INCONTINENCE, and damage to the nerves that supply the penis resulting in ERECTILE DYSFUNCTION.

Radical prostatectomy Radical prostatectomy is a treatment for prostate cancer in which the surgeon removes the prostate gland, seminal vesicles, and surrounding tissue (fat, MUSCLE, and connective tissue) during an operation that can take five hours or longer. Often the surgeon removes adjacent lymph nodes as well. Radical prostatectomy is major surgery that requires about 10 days in the hospital and up to four months for recovery. Radical prostatectomy is treatment for prostate cancer and has a high risk for complications such as urinary incontinence and erectile dysfunction, though these complications may improve over time.

In some circumstances the surgeon may opt to perform radical prostatectomy laparoscopically, inserting a laparoscope and surgical instruments through several small incisions in the abdomen. The laparoscopic approach significantly lessens the risk for complications and shortens recovery time, though the operation is nonetheless major surgery. Sometimes the surgeon may use laparoscopic surgery to remove pelvic lymph nodes while using the open perineal approach to remove the prostate gland.

Risks and Complications

Prostatectomy, particularly an open or radical approach, is extensive surgery with potential complications that require careful consideration. Among them are excessive bleeding during or after surgery that may necessitate BLOOD TRANSFUSION, INFECTION, retrograde ejaculation, urinary incontinence, bladder damage, rectal damage, and erectile dysfunction. Generalized risks include reaction to ANESTHESIA and blood clots. The risk for complications depends on the reason for the prostatectomy (cancer or noncancerous condition), the type of operation, age, and overall health status. Surgeons prescribe prophylactic antibiotics to help prevent infection and antiembolism therapies such as ANTICOAGULATION THERAPY and compression stockings or boots to help prevent blood clots.

Outlook and Lifestyle Modifications

For many men, prostatectomy ends the symptoms of the condition that necessitated the operation. Because the prostate gland continues to slowly enlarge as a man ages, about 20 percent of men who have TURP to treat BPH find their symptoms return in 10 to 15 years, requiring additional treatment. Many men are able to return to normal activities, including sexual activities, within a few months of their surgeries. However, prostate cancer may require adjuvant (follow-up or accompanying) treatment after surgery.

See also ANTIBIOTIC PROPHYLAXIS; CANCER TREATMENT OPTIONS AND DECISIONS; SURGERY BENEFIT AND RISK ASSESSMENT.

prostate-specific antigen (PSA) An enzyme PROSTATE GLAND cells produce. Prostatic fluid, the cumulative secretions of prostate gland cells, contains high levels of PSA. PSA acts on the jellylike substance that encases SPERM during their storage in the seminal vesicles, liquefying the substance when the sperm mix with prostatic fluid in the URETHRA during EJACULATION. This action restores motility to the sperm.

Measuring the BLOOD concentration of PSA provides information about the health status of the prostate gland. In the healthy prostate gland of a man under age 40, the prostate gland cells form a tight structure that directs nearly all PSA the cells produce into the prostatic fluid; only a small amount of PSA escapes to circulate in the blood. In certain health conditions, most notably PROSTATE CANCER, PSA blood levels rise. Prostate cancer disrupts the structure and organization of prostate gland cells, allowing much higher concentrations of PSA to enter the blood circulation. Other health conditions such as PROSTATITIS, BENIGN PROSTATIC HYPERPLASIA (BPH), and even URINARY TRACT INFECTION (UTI) can also cause PSA levels to rise.

As well, PSA also normally rises with increasing age because the prostate gland slowly enlarges beginning around age 40, a process that also alters the structure and organization of prostate gland cells. Because of this natural change, normal PSA blood values differ according to a man's age. Blood PSA concentrations above the value for age may suggest the presence of prostate disease, including prostate cancer. In general, a blood PSA level of 4 nanograms per milliliter (ng/mL) may indicate the need for further evaluation of the prostate gland's health.

NORMAL VALUES FOR BLOOD PROSTATE-SPECIFIC ANTIGEN (PSA) LEVELS

Age	PSA Blood Concentration
40 to 49	< 2.5 nanograms per milliliter (ng/mL)
50 to 59	< 3.5 ng/mL
60 to 69	< 4.5 ng/mL
70 to 79	< 6.5 ng/mL

However, health experts disagree about the value of blood PSA levels for prostate cancer screening and detection. There is limited consensus around what the values mean, there are several methods for measuring PSA that are not equivalent to one another, and there is a higher rate of false-positive PSA results—PSA levels that are elevated for reasons other than prostate disease—than many doctors find acceptable. These factors are of concern because the next step of diagnosis, biopsy, is invasive and carries risk for numerous complications. Many doctors find PSA blood tests more useful when treating disorders of the prostate gland, such as BPH and prostate cancer, as measures to help assess the effectiveness of treatment.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CANCER PREVENTION.

prostatitis INFLAMMATION, INFECTION, or PAIN of the PROSTATE GLAND. Prostatitis may be acute (come on suddenly) or chronic (persist or recur over time). Urologists classify five types of prostatitis:

- Acute bacterial prostatitis occurs as a result of infection with BACTERIA, usually URINARY TRACT INFECTION (UTI), that infiltrates the prostate gland. SEXUALLY TRANSMITTED DISEASES (STDS), notably GONORRHEA and CHLAMYDIA, may also cause acute bacterial prostatitis. Treatment with appropriate ANTIBIOTIC MEDICATIONS usually cures the infection.
- Chronic bacterial prostatitis occurs as a result of an underlying chronic health condition that allows continued or repeated bacterial access to the prostate gland. Treatment requires long-term, and sometimes repeated, antibiotic therapy as well as efforts to resolve the underlying condition.
- Chronic inflammatory prostatitis causes pain and exists when there is inflammation but no infection. Treatment is with NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) to reduce inflammation and relieve pain.
- Asymptomatic inflammatory prostatitis does not cause any symptoms and is sometimes a factor in male INFERTILITY that shows up during FERTILITY testing. NSAIDs may improve the inflammation.
- Prostadynia, also called chronic noninflammatory prostatitis, involves neither inflammation nor infection though pain is persistent and sometimes debilitating. Doctors do not know what causes prostadynia. Medications such as alpha blockers, used to treat BENIGN PROSTATIC HYPERPLASIA (BPH), and NSAIDs sometimes provide relief. BIOFEEDBACK, ACUPUNCTURE, and prostatic massage are other methods to relieve pain.

Symptoms and Diagnostic Path

The primary symptom of all but asymptomatic inflammatory prostatitis is pain in the lower pelvis. Men who have acute bacterial infection often have FEVER and feel quite ill. Men who have chronic bacterial prostatitis may feel intermittently fatigued. The diagnostic path for prostatitis may include DIGITAL RECTAL EXAMINATION (DRE) to palpate the prostate gland, measurement of BLOOD PROSTATE-SPECIFIC ANTIGEN (PSA) levels, urinalysis including urine culture, and SEMEN analysis to look for the presence of red blood cells (evidence of bleeding), white blood cells (evidence of inflammation), and bacteria (evidence of infection). When symptoms are chronic, additional diagnostic procedures may include transrectal ULTRASOUND (TRUS), COMPUTED TOMOGRAPHY (CT) SCAN, prostate biopsy, or CYSTOSCOPY.

Treatment Options and Outlook

Treatment and outlook depend on the identified underlying cause for the symptoms. Because the structure of the glandular tissue within the prostate gland is such that it prevents blood components from entering the prostate gland (a protective mechanism to prevent ANTIBODY formation and to keep the semen PSA concentration high), the course of antibiotic therapy for bacterial prostatitis is lengthy, typically four to eight weeks. A complication of untreated or undertreated bacterial prostatitis is prostatic ABSCESS (the formation of a contained pocket of pus), which may require a cystoscopic procedure under ANESTHESIA to drain the abscess.

Risk Factors and Preventive Measures

Prompt diagnosis and treatment of UTIs and STDs significantly reduce the risk for bacterial prostatitis. There are no clear preventive measures for other forms of prostatitis.

See also CHRONIC PAIN; CYSTITIS; MALDYNIA; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; URETHRITIS.

puberty The transition from childhood to the sexual and reproductive maturity that marks adulthood. Puberty occurs under the influence of hormonal shifts. The path of puberty tends to start and end about two years earlier for girls than for boys. Puberty in most industrialized parts of the world begins between ages 10 to 15 and concludes between ages 17 to 19. SECONDARY SEXUAL CHARACTERISTICS emerge during puberty, coinciding with ADOLESCENCE, the emotional and psychologic changes that occur during the shift from childhood to adulthood.

Puberty begins with hormonal changes the HYPOTHALAMUS and the PITUITARY GLAND initiate that stimulate the gonads (ovaries in women and testicles in men) to begin producing gonadotropins (sex hormones)—ESTROGENS and ANDROGENS. The PINEAL GLAND, which regulates the body's circadian rhythms, also appears to play a role. Researchers do not know what triggers these changes. Because external factors such as nutritional status and illness can influence the timing of puberty, researchers suspect body mass (height and weight) may somehow signal the endocrine system. CHROMOSOMAL DISORDERS involving the sex chromosomes, such as TURNER'S SYNDROME, which affects girls, and KLINEFELTER'S SYNDROME, which affects boys, alter or prevent natural puberty.

In both sexes, the first indication of puberty is the growth of HAIR under the arms and around the GENITALIA. At first the hair is light and fine; as puberty progresses the hair darkens and thickens. Hair on the legs also darkens and becomes more dense. There is usually an accompanying growth spurt, which in boys particularly may amount to six inches or more of height within a year. Boys begin to broaden at the shoulders and girls at the hips during this surge of growth. The remaining changes that occur with puberty are gender specific.

Puberty in Girls

BREAST buds, firm bumps that form beneath the nipples, mark the onset of estrogen-driven changes occurring in the girl's body. In most girls breast budding occurs simultaneously with the development of pubic and axillary hair though one set of events may precede the other. Over the course of one to three years the breasts continue to grow and take form and the girl's body takes on a womanly appearance. Generally, about the time the pattern of body hair becomes adult-like the girl begins to menstruate, indicating her ovaries are mature and functional. Puberty concludes in girls when the MENSTRUAL CYCLE is regular and predictable. External factors that can influence the start of MENSTRUATION (MENARCHE) include OBESITY, which tends to cause earlier menarche, and intense physical activity such as athletic competition, which tends to cause later menarche. Both are within the range of normal.

Puberty in Boys

Enlargement of the SCROTUM and testicles marks the onset of TESTOSTERONE-driven changes occurring in the boy's body. The boy's voice lowers in register and deepens. Growth continues at a rapid rate. Over the course of one to three years the PENIS thickens and elongates, and the testicles begin producing SPERM. Sexually stimulated ERECTION and NOCTURNAL EMISSION ("wet dreams") are common. Toward the conclusion of puberty hair on the arms may also become darker, longer, and more dense, and hair begins to grow on the chest. Puberty concludes in boys when the genitalia reach adult proportions, which occurs at age 15 to 19.

Precocious Puberty

Occasionally disturbances of hormonal function may result in early, or precocious, puberty, which doctors define as the onset of puberty before age 8 in girls and age 9 in boys. Treatment for precocious puberty depends on the underlying cause of the hormonal disturbance when the doctor can identify it; a common cause is pituitary ADENOMA (noncancerous tumor in the pituitary gland). Often the cause remains unknown (idiopathic precocious puberty), in which case the doctor may administer GONADOTROPIN-RELEASING HORMONE (GNRH) to regulate the pituitary gland's release of LUTEINIZING HORMONE (LH), the hormone that stimulates estrogen and testosterone. There are usually no adverse effects of idiopathic precocious puberty.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; HYPOGONADISM.

retrograde ejaculation A circumstance in which a man's SEMEN enters the BLADDER instead of ejecting from the PENIS during EJACULATION. Semen and URINE share the URETHRA for their exit from a man's body. A tiny valve in the urethra at the neck of the bladder ordinarily closes across the entry to the bladder during ejaculation, directing the flow of semen through the penis. When this valve does not close, semen takes the path of least resistance and enters the bladder during ejaculation. A man may notice retrograde ejaculation as a "dry ORGASM" in which very little discharge leaves the penis with orgasm. Retrograde ejaculation does not present any health concerns for the man

though results in INFERTILITY when all semen enters the bladder. Analysis of the first urine after ejaculation shows the presence of SPERM. That first urine after ejaculation may also appear cloudy.

BENIGN PROSTATIC HYPERPLASIA (BPH), a noncancerous enlargement of the PROSTATE GLAND, is the most common cause of retrograde ejaculation. The prostate gland surrounds the neck of the bladder; in BPH the gland may compress the urethra in such a way as to prevent the valve from properly functioning. Surgery to treat BPH or PROSTATE CANCER may permanently damage or remove the valve. Retrograde ejaculation may also occur in men who have DIABETES, particularly when BLOOD GLUCOSE (sugar) regulation is poor. Some medications that affect smooth MUSCLE function may also cause retrograde ejaculation. When the cause is a medication SIDE EFFECT, ejaculation returns to normal when the man stops taking the medication. When the cause is a health condition such as BPH or diabetes, retrograde ejaculation is likely not reversible.

See also FERTILITY; PROSTATE HEALTH; SEXUAL HEALTH; URINARY TRACT INFECTION (UTI).

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scrotum The saclike structure, a thin layer of MUSCLE and SKIN, suspended from the base of a man's pelvis that contains the TESTICLES. A pair of ligaments, the spermatic cords, extend from the lower abdomen to support the scrotum. The spermatic cords also serve as the conduits for the BLOOD vessels and nerves that supply the testicles. The abdominal and scrotal muscles contract or relax to raise or lower the scrotum, maintaining the appropriate temperature for spermatogenesis (SPERM production). Sperm production, which is a key function of the testicles, requires a temperature of 96°F to 96.5°F, about 2 degrees lower than body temperature. Pubic HAIR covers the outside of the scrotum after PUBERTY.

See also HERNIA; SPERMATOCELE; VARICOCELE.

secondary sexual characteristics The physical changes that distinguish the genders from each other. Secondary sexual characteristics emerge with PUBERTY and establish sexual and reproductive maturity: males produce viable SPERM capable of causing PREGNANCY, and females produce ripened OVA (eggs) capable of fertilization that results in pregnancy.

FEMALE SECONDARY SEXUAL CHARACTERISTICS

growth of pubic and axillary (underarm) HAIR
thickened and coarse or dark leg hair
enlarged breasts and broadened hips

MALE SECONDARY SEXUAL CHARACTERISTICS

growth of pubic, axillary, chest and facial hair
thickened, darkened, and coarse arm and leg hair
broadened shoulders and chest
increased MUSCLE mass and definition
deepened voice and prominent Adam's apple in the THROAT
enlarged TESTICLES, enlarged and elongated PENIS

See also CONCEPTION; CONTRACEPTION; FERTILITY; MENSTRUAL CYCLE; MENSTRUATION; PREGNANCY.

semen The fluid of a man's EJACULATION. In a fertile man about 5 percent of the semen content is SPERM; in a man who has had a VASECTOMY semen does not contain sperm. The seminal vesicles and the PROSTATE GLAND produce the milky fluid of semen, which is primarily a water base that contains proteins, sugars (notably fructose and some GLUCOSE), lipids (fatty acids), electrolytes, and PROSTAGLANDINS. The bulbourethral glands, also called Cowper's glands, add a gelatinous secretion to the semen that thickens it. Semen may flow back into the BLADDER rather than out of the PENIS (RETROGRADE EJACULATION) in a man with a PROSTATECTOMY (surgery to remove the prostate gland).

The electrolytes protect sperm on their journey through the VAGINA and into the UTERUS. The sugars, particularly fructose, and lipids provide nutrition for the sperm. Vaginal secretions are highly acidic and deadly to sperm. The thickness of semen helps contain and insulate sperm as they travel through the VAGINA, though the semen thins by the time it reaches the UTERUS to release the sperm. The electrolytes in semen make it highly alkaline, helping neutralize the vaginal environment to improve sperm survival. Prostaglandins help suppress the IMMUNE RESPONSE, the natural reaction of the woman's IMMUNE SYSTEM to the presence of the sperm. The semen also has the ability to carry various pathogens such as viruses and BACTERIA that can spread SEXUALLY TRANSMITTED DISEASES (STDS).

Semen analysis is a laboratory examination of a semen sample to measure the concentrations of its ingredients and the number and characteristics of the sperm. ALCOHOL consumption, cigarette smok-

ing, and frequency of ejaculation are among the factors that influence the volume and content of semen.

SEMEN NORMAL VALUES PER EJACULATION	
semen volume	1.5 to 6.5 milliliters
sperm count	20 to 250 million per milliliter
pH	7.1 to 8.0
fructose	30 milligrams per milliliter

See also CONTRACEPTION; HEMATOSPERMIA; HYDROCELE; PATHOGEN; SEXUAL INTERCOURSE; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; VARICOCELE; VIRUS.

sexual dysfunction Physical or psychologic circumstances that interfere with sexual interest or sexual activity. Most people experience some degree of sexual dysfunction over the course of their lifetimes. The causes of sexual dysfunction are numerous; most are transient (improve or go away with time). Physical illness, injury, surgery, disability, medication side effects, emotional stress, job pressures, CHILDBIRTH and PARENTING responsibilities, GRIEF, DEPRESSION, and relationship discord are among the most common factors. People who have experienced SEXUAL ASSAULT or rape, in childhood or as adults, may also have difficulty establishing or maintaining healthy sexual relationships. As well, an individual's attitudes toward and understanding of sex affect the nature and quality of sexual interaction.

Painful SEXUAL INTERCOURSE, called DYSPAREUNIA, is the most common form of physical sexual dysfunction in women. Dyspareunia may result from insufficient vaginal lubrication (which becomes more common after MENOPAUSE), vaginal MUSCLE spasms (VAGINISMUS), INFLAMMATION or irritation of the VAGINA (VAGINITIS) or VULVA (vulvitis), PAIN in the external GENITALIA (VULVODYNIA), UTERINE PROLAPSE, ENDOMETRIOSIS, UTERINE FIBROIDS, or perineal injury (such as perineal tear or EPISIOTOMY repair). Chronic PELVIC INFLAMMATORY DISEASE (PID) may also cause pain during sex. Psychologic or emotional factors may also contribute to dyspareunia.

The most common form of physical sexual dysfunction in men is the inability to achieve or maintain an ERECTION (ERECTILE DYSFUNCTION), which may result from physical or psychologic factors. ATHEROSCLEROSIS (accumulation of plaque deposits in the arteries that narrows the channel for BLOOD flow), DIABETES, peripheral NEUROPATHY (damage to the small nerves that supply the penis), long-term cigarette smoking, and medication side effects are the leading physical causes of erectile dysfunction in men. Men may also experience pain with intercourse as a consequence of URETHRITIS, PEYRONIE'S DISEASE, and inadequate lubrication during penetration.

Excessive ALCOHOL use, ILLICIT DRUG USE, and heavy or long-term cigarette smoking contribute to sexual dysfunction in men and women. Alcohol and many drugs, prescription or "street," depress LIBIDO. Alcohol affects the health of blood vessels and nerves; long-term alcohol abuse is another cause of erectile dysfunction in men. Cigarette smoking also affects blood flow; NICOTINE is a powerful vasoconstrictor (narrows blood vessels) and the changes in blood oxygen levels that occur when smoking affect the function of cells throughout the body. These effects are most significant for NERVE cells, which require consistent levels of oxygen.

Symptoms and Diagnostic Path

The primary symptom of sexual dysfunction is the reduced ability to engage in or enjoy sexual activity. Men and women may experience difficulty achieving ORGASM (sexual climax); this is more common in women. Psychologic and emotional symptoms of sexual dysfunction in men or women may include diminished libido (sex drive), disinterest in sex, or excessive interest in sex. The diagnostic path begins with a comprehensive medical examination, including PELVIC EXAMINATION for women, and discussion about factors that might be contributing to the symptoms. The doctor may perform additional diagnostic procedures, depending on the findings of the medical examination, such as blood tests (men and women), cultures of vaginal fluids (women) or any discharges (men and women), or pelvic ULTRASOUND (women).

Treatment Options and Outlook

Treatment options depend on the identified causes of the symptoms. Treatment may be as straightforward as changing or stopping a medication that is causing the symptoms or treating an underlying physical condition. Often the symptoms of sexual

dysfunction resolve when the factors responsible for them go away, such as when a person changes from a high-pressure job to one that has a lower level of stress. Sometimes simply the process of discussing life circumstances in response to the doctor's questioning provides a connection between the circumstances and the symptoms that the person had not been able to see.

Sexual dysfunction can be a complex intertwining of physical and psychologic factors that benefits from a combination of treatment for the physical conditions and therapy (counseling) for the psychologic and emotional factors. Relationship or personal therapy may help a person come to insight and understanding about his or her attitudes and expectations about sex.

Risk Factors and Preventive Measures

The key risk factors for sexual dysfunction are physical or psychologic conditions or emotional issues that affect interest in and satisfaction with sexual activity. Appropriate treatment combined with open and compassionate communication can help partners address their concerns and achieve a level of sexual interaction that accommodates each partner's needs. Though it is not always possible to prevent health and life circumstances from resulting in sexual dysfunction, most causes of sexual dysfunction are treatable.

See also ALCOHOLISM; EJACULATION; FERTILITY; INFERTILITY; PARAPHIMOSIS; PELVIC INFLAMMATORY DISEASE (PID); PHIMOSIS; PRIAPISM; RETROGRADE EJACULATION; SEXUAL HEALTH.

sexual health Measures men and women can take to experience sexuality in ways that support their physical and emotional well-being. A key factor for sexual health is overall health—nutritional EATING HABITS, daily physical exercise, MEDITATION or relaxation, adequate sleep, and adequate time for leisure or recreational activities. Sexual health further incorporates measures to reduce the risk for health conditions specifically related to sexual activity such as INFECTION with SEXUALLY TRANSMITTED DISEASES (STDS) and undesired PREGNANCY (CONTRACEPTION).

In addition to the physical factors of sexual health are the psychologic, emotional, and social factors. Despite the tendency of health-care providers to focus on physical concerns such as STDs because of the health issues these infections entail, the emotional intimacy of sexual relationships is an essential component of sexual health. It is sometimes difficult to determine when a relationship is consenting and when it is abusive. Sexual health requires mutual appreciation for each partner's needs, physical and emotional.

Young people especially may face pressure to enter into sexual relationships yet are uncertain that they are ready or willing to do so. The consequences may be far reaching. One million teens become pregnant in the United States each year. STDs such as GENITAL HERPES, HEPATITIS B, and hepatitis C are treatable but not curable. Though treatment regimens now greatly extend life and improve quality of life, HIV/AIDS remains ultimately fatal. Other STDs may cause scarring and other damage that results in permanent INFERTILITY.

See also BREAST HEALTH; BREAST SELF-EXAMINATION (BSE); PROSTATE HEALTH; SEXUAL ASSAULT; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; TESTICULAR SELF-EXAMINATION (TSE).

sexual intercourse Sexual activity that involves penetration between sexual partners. In conventional context sexual intercourse is the insertion of a man's erect PENIS into a woman's VAGINA and is the primary mechanism of human reproduction. Male EJACULATION propels SEMEN into the vagina, where the SPERM it contains may unite with an egg (ovum) if the woman is ovulating and conditions are conducive. In contemporary context the term more broadly encompasses vaginal sex, anal sex, and oral sex between partners of either gender as acts of intimacy and pleasure, physical and emotional, that may or may not include the intent to conceive a PREGNANCY.

See also CONCEPTION; CONTRACEPTION; ORGASM; OVULATION; SEXUAL ASSAULT; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

sexually transmitted diseases (STDs) Infections that spread from one person to another during sexual activity, causing illness or damage to the body. The pathogens that cause STDs may be BACTERIA, viruses, or parasites. STDs, also called sexually transmitted infections (STIs), are significant concerns worldwide, diminishing overall health

and QUALITY OF LIFE. STDs infect tens of millions of people in the United States and hundreds of millions of people throughout the world.

STDs may not have symptoms though the person continues to be infectious (capable of passing the STD to sex partners). Often a person has more than one STD at the same time, a circumstance called co-infection. It is possible for reinfection with the same STD to occur after treatment. ANTIBIOTIC MEDICATIONS are the mainstay of treatment for bacterial STDs. ANTIVIRAL MEDICATIONS may alleviate symptoms in viral STDs such as GENITAL HERPES and lessen the risk for transmitting the VIRUS to others, though the virus often remains in the body and symptoms recur.

Though all STDs are treatable, many are not curable. Some, such as HEPATITIS B and HUMAN PAPILLOMAVIRUS (HPV), are known causes of cancer (LIVER CANCER and CERVICAL CANCER, respectively). Hepatitis C may be fatal and at present HIV/AIDS is always fatal, though treatment and supportive lifestyle measures can manage both conditions for years to decades. STDs are a leading cause of PELVIC INFLAMMATORY DISEASE (PID) in women, a serious INFECTION that can result in INFERTILITY by causing scarring and occlusion (blockage) of the FALLOPIAN TUBES and sometimes the CERVIX.

Oral contraceptives (birth control pills), intrauterine devices (IUDs), cervical diaphragms, spermicides, VASECTOMY, TUBAL LIGATION, and HYSTERECTOMY, though effective methods of CONTRACEPTION, do not prevent INFECTION with SEXUALLY TRANSMITTED DISEASES (STDS).

Abstinence (no sexual partners) is the most effective means to prevent infection with STDs. Among people who are sexually active, key measures to reduce the risk for STD infection are

- long-term, mutual monogamy (one exclusive sex partner)
- male latex condom use with every sexual act (vaginal intercourse, anal intercourse, oral sex, partner MASTURBATION)

The effectiveness of these measures varies for the specific STD. Latex condoms are highly effective for preventing GONORRHEA and HPV, for example, though may be less effective for protecting against genital herpes and HIV/AIDS. The female condom is another barrier method of CONTRACEPTION that provides some, but more limited, protection from STD infection compared to the male condom. Unprotected contact with bodily fluids (pre-ejaculate or vaginal secretions), such as may occur during heavy petting and foreplay, carries the same risk for STD infection as does actual intercourse.

Infections not typically characterized as STDs, such as TUBERCULOSIS, may also pass between people during sexual activity. Conversely, some infections characteristically transmitted through sexual contact may also pass via other means such as shared needles among intravenous DRUG users (notably HIV/AIDS and hepatitis). An infant may acquire gonorrhea, CHLAMYDIA, and genital herpes during CHILDBIRTH (passage through the VAGINA). An infant may also acquire congenital herpes without passing through the birth canal if the mother first becomes infected when she is pregnant.

Because many STDs are highly contagious and prompt treatment can minimize their spread as well as prevent long-term health complications for infected individuals, health experts strongly encourage diagnostic testing and treatment for all sexual partners of everyone who acquires an STD. In the United States, community health centers and public health services provide low-cost or free STD testing and treatment. Private doctors and other health-care providers also diagnose and treat STDs.

See also ANTIBIOTIC RESISTANCE; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

sperm The male cells of reproduction, also called gametes. A spermatozoon (single sperm cell) is a haploid cell; it contains one half of the genetic material necessary for human life. The epididymis within the testicle (also called the testis) produces sperm, a process called spermatogenesis, at the rate of hundreds of millions each day from PUBERTY (the onset of sexual maturity) through the end of life. The tissues of the TESTICLES absorb sperm that remain in the epididymis for longer than six weeks, allowing the supply of sperm to remain fresh.

Spermatogenesis The production of new sperm cells begins with the division and differentiation of

SEXUALLY TRANSMITTED DISEASES (STDS)

STD	Cause	Symptoms	Treatment and Outlook
CHLAMYDIA	BACTERIA: *Chlamydia trachomatis*	often no symptoms; men may have discharge from PENIS and burning with URINATION; women may have vaginal discharge	treatable and curable with antibiotic medications
GENITAL HERPES	VIRUS: HERPES SIMPLEX 2 (HSV-2)	burning, itching, chancrelike sores; vaginal discharge in women; burning with urination in men	not curable but symptom relief with ANTIVIRAL MEDICATIONS
GONORRHEA	bacteria: *Neisseria gonorrhoeae*	often no symptoms; burning with urination and discharge from the penis in men; vaginal discharge in women	treatable and curable with antibiotic medications though some strains are resistant
HEPATITIS B	virus: hepatitis B virus (HBV)	JAUNDICE, FEVER, NAUSEA, VOMITING, swollen and tender LIVER	preventable with hepatitis B VACCINE postexposure prophylaxis
hepatitis C	virus: hepatitis C virus (HCV)	jaundice, fever, nausea, vomiting, swollen and tender liver	postexposure prophylaxis
HIV/AIDS	virus: human immunodeficiency virus (HIV)	flulike symptoms when INFECTION occurs; typically no symptoms until AIDS emerges	not curable and ultimately fatal; antiretroviral drugs can keep the virus in check for delay of disease manifestation and remission of symptoms
HUMAN PAPILLOMAVIRUS (HPV)	virus: human papillomavirus (HPV)	often no symptoms; may cause genital warts	not curable though infection often runs its course in several years; various methods to remove warts; some strains associated with CERVICAL CANCER
nongonorrheal URETHRITIS	bacteria: various	burning with urination; discharge from the penis in men	treatable and curable with antibiotic medications
SYPHILIS	bacteria: *Treponema pallidum*	painless chancre that may be unnoticeable; SKIN RASH; fever; late stage symptoms often systemic	treatable and curable with antibiotic medications
TRICHOMONIASIS	PROTOZOA: *Trichomonas vaginalis*	foul-smelling, discolored discharge; painful urination in men; vaginal or vulvar itching or burning in women	treatable and curable with metronidazole

germ cells in the seminiferous tubules. Specialized cells called Sertoli cells nourish and protect the new sperm cells, ushering them into the epididymis where they grow to maturity as they migrate through the 10 to 12 feet of tightly coiled tubule that makes up this testicular structure. Their journey takes sperm to the ejaculatory ducts, where they mix with SEMEN. A mature spermatozoon consists of a head (the cell body) containing genetic material and a whiplike tail that

provides mobility. ANDROGENS, notably TESTOSTERONE, and other hormones regulate spermatogenesis. Spermatogenesis is a continuous process.

Fertilization The role of the sperm is to fertilize the ovum (egg), the first step in establishing PREGNANCY. SEXUAL INTERCOURSE, in which the man's erect PENIS enters the woman's VAGINA, is the natural mechanism through which sperm gain access to the woman's reproductive tract. From 20 to 250 million sperm leave the testicles within the semen, the fluid that nourishes and protects the sperm, during each EJACULATION. The sperm swim through the fluids in the vagina, enter the UTERUS through the CERVIX, and continue to the entrance of the FALLOPIAN TUBES at the top of the uterus.

Of the millions of sperm that begin this journey, most die before reaching the fallopian tube. Surviving sperm continue through the fallopian tube; fertilization takes place if there is an ovum (egg) also in the fallopian tube and a sperm is able to penetrate its surface membrane. Multiple factors influence this ability, including the shape of the sperm head, the remaining motility of the sperm tail to thrust the head through the ovum's membrane, and the environment within the fallopian tube. Once a single sperm penetrates the shell of the ovum, the ovum closes itself to further penetration. Only the head of the sperm enters the ovum; the tail of the sperm drops off outside the ovum. Multiple pregnancies occur when two or more sperm simultaneously penetrate the ovum (identical multiples) or when two or more OVA are present in the fallopian tubes (fraternal multiples). Abnormalities of sperm structure or motility may interfere with the sperm's ability to reach or penetrate the ovum.

For further discussion of sperm within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); CELL STRUCTURE AND FUNCTION; FERTILITY; INFERTILITY; SECONDARY SEXUAL CHARACTERISTICS; SEXUAL HEALTH.

spermatocele A cyst containing dead SPERM that forms in the epididymis. Doctors do not know what causes spermatoceles, also called epididymal cysts, to develop though suspect they result from some sort of obstruction that blocks their flow through the epididymis. A spermatocele is round, firm, and clearly defined. A man may discover a spermatocele during routine TESTICULAR SELF-EXAMINATION (TSE) or the doctor may find it during ROUTINE MEDICAL EXAMINATION. A large spermatocele may cause PAIN. ULTRASOUND of the SCROTUM confirms the diagnosis. No treatment is necessary for a small spermatocele that does not cause symptoms. For large spermatoceles or spermatoceles that cause pain, surgery to remove the spermatocele is the most effective treatment. However, surgery may impair FERTILITY because it usually involves removing a portion of the epididymis.

See also HYDROCELE; SURGERY BENEFIT AND RISK ASSESSMENT; VARICOCELE.

sperm donation The collection of a man's SEMEN, which contains SPERM, for use in FERTILITY treatments. The man obtains the semen for donation through MASTURBATION to produce EJACULATION. Sperm banks (facilities that collect and store donated sperm) have varying policies for qualifying sperm donors. In general a sperm donor must be between the ages of 18 and 45, have no known genetic or hereditary conditions, and have no exposure to infectious diseases such as HIV/AIDS, HEPATITIS, and SEXUALLY TRANSMITTED DISEASES (STDS). Sperm donors have no legal rights or responsibilities for children conceived with their sperm and typically remain anonymous.

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); GESTATIONAL SURROGACY.

stillbirth The death of the FETUS after 24 weeks of gestation. There are numerous causes for stillbirth; often the reason remains unknown. Sometimes the obstetrician cannot detect the fetal heartbeat during a routine PRENATAL CARE visit; more often the woman notices the fetus has stopped moving. An ULTRASOUND can confirm the death, after which the doctor induces labor to deliver the baby. Death may also occur during CHILDBIRTH. The loss of a PREGNANCY through stillbirth is emotionally traumatic for parents, family members, and friends.

See also ABORTION; GRIEF; PREMATURE BIRTH; SUPPORT GROUPS.

T

testicles The paired male organs, also called the male gonads, that produce SPERM and ANDROGENS, notably TESTOSTERONE. Each egg-shaped testicle is about two inches long and an inch in diameter. A man's testicles may be slightly different from each other in size. The testicles reside side by side in the SCROTUM, a saclike structure suspended outside the body from the lower pelvis. The testicles are outside the body because spermatogenesis (the generation, or production, of sperm) requires a temperature two to three degrees below normal body temperature. A hollow ligament, the spermatic cord, extends from the abdomen to the testicle through the inguinal canal, carrying the ARTERY, VEIN, LYMPH structures, and nerves that supply the testicle.

The outer layer of the testicle is the tunica albuginea, a sheath of fibrous tissue that contains and protects the structures within the testicle. Tightly coiled tubules, the seminiferous tubules and the epididymis, make up the main mass of the testicle. The cells that fill the space between the tubules are the Leydig cells, also called the interstitial cells, which produce testosterone. The seminiferous tubules contain germ cells, from which new sperm cells (spermatozoa) arise, and Sertoli cells, which nourish and support the developing sperm cells. The Sertoli cells draw testosterone into the seminiferous tubules, which sperm cells require to come to maturation, and prevent antibodies in the BLOOD from entering the seminiferous tubules.

As the sperm cells develop, they travel from the seminiferous tubules to the epididymis, another coiled tubule. The epididymis incubates spermatozoa to maturity during the 12 days or so it takes for them to journey through the convolutions of the epididymis, during which they acquire tails and motility (the ability to move). The vas deferens then carries sperm from the epididymis to the ejaculatory duct, which is within the lower pelvis.

HEALTH CONDITIONS THAT CAN AFFECT THE TESTICLES

CRYPTORCHIDISM	EPIDIDYMITIS
GENITAL TRAUMA	HYDROCELE
HYPOGONADISM	INFERTILITY
KLINEFELTER'S SYNDROME	ORCHITIS
SPERMATOCELE	TESTICULAR CANCER
TESTICULAR TORSION	VARICOCELE

For further discussion of the testicles within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System." For further discussion of the testicles within the context of the structures and functions of the endocrine, system please see the overview section "The Endocrine System."

See also CONCEPTION; CONTRACEPTION; ORCHIECTOMY; ORCHIOPEXY; PROSTATE GLAND; SEXUAL HEALTH; VAS DEFERENS; VASECTOMY.

testicular cancer A malignant (cancerous) tumor that arises from the tissue of a man's testicle. Testicular cancer is usually unilateral (occurs only in one testicle), though sometimes occurs bilaterally (in both TESTICLES), and is most common in early adulthood (ages 20 to 34). With detection before the cancer metastasizes (spreads elsewhere in the body), the cure rate for testicular cancer is 99 percent. Doctors in the United States diagnose testicular cancer in about 8,000 men each year.

The two main types of testicular cancer are seminoma and nonseminoma, though some testicular cancers contain a mix of these types. Oncologists classify mixed testicular cancer tumors as nonseminoma because the nonseminoma cells

tend to be dominant in determining the tumor's behavior. The distinction is important because the types have different patterns of aggressiveness (rate and way in which the tumor grows), METASTASIS, and responsiveness to treatment.

Symptoms and Diagnostic Path

The most common symptom of testicular cancer is a painless though sometimes tender lump or swelling in the SCROTUM. The man may discover the lump or swelling during TESTICULAR SELF-EXAMINATION (TSE) or coincidentally, or the doctor may find it during ROUTINE MEDICAL EXAMINATION. Testicular cancer also may cause few symptoms until it has grown and spread outside the testicle, such as to organs in the abdomen. In such circumstances, symptoms may be more generalized and include low pelvic or low back heaviness or pressure, fatigue, and overall sense of not feeling well (malaise).

BASIC STAGING OF TESTICULAR CANCER

Stage	Meaning	Treatment Options
stage 0/carcinoma in situ	cancer remains contained in the cells of their origin	radical inguinal ORCHIECTOMY
stage 1	cancer remains confined to a local tumor in one testicle	radical inguinal orchiectomy seminoma: inguinal and retroperitoneal LYMPH NODE irradiation nonseminoma: retroperitoneal lymph node dissection or two cycles of chemotherapy
stage 2 nonbulky	cancer has spread to retroperitoneal LYMPH nodes and nodes are 2 inches or smaller	radical inguinal orchiectomy seminoma: inguinal and retroperitoneal lymph node irradiation nonseminoma: retroperitoneal lymph node dissection, then two cycles of chemotherapy
stage 2 bulky	cancer has spread to retroperitoneal lymph nodes and nodes are larger than 2 inches	radical inguinal orchiectomy seminoma: three cycles of chemotherapy nonseminoma: three or four cycles of chemotherapy
stage 3 nonbulky	cancer has spread to lymph nodes outside the abdomen and to the LUNGS though all metastasized tumors are ¾ inch or smaller	radical inguinal orchiectomy seminoma: three or four cycles of chemotherapy; RADIATION THERAPY for BRAIN METASTASIS nonseminoma: three or four cycles of chemotherapy; surgery to remove any remaining metastatic tumors
stage 3 bulky	cancer has spread to lymph nodes outside the abdomen and nonlung sites such as the LIVER or brain, and some metastasized tumors are larger than ¾ inch	radical inguinal orchiectomy seminoma: four cycles of chemotherapy; radiation therapy for brain metastasis nonseminoma: four cycles of chemotherapy; surgery to remove any remaining metastatic tumors clinical trials
stage 4/recurrent	cancer has returned after treatment	surgery for small, isolated metastases high-DOSE chemotherapy

The diagnostic path typically includes BLOOD tests to look for TUMOR MARKERS (proteins in the blood circulation that suggest the presence of cancer), such as ALPHA FETOPROTEIN (AFP) and lactate dehydrogenase (LDH), and ULTRASOUND of the scrotum, which may indicate whether the growth is fluid-filled (more likely a cyst or HYDROCELE) or solid (more likely a tumor).

Though biopsy (removal of a sample of the tumor's tissue for laboratory examination) is the means of establishing a cancer diagnosis in most other types of cancer, the risk that the biopsy will cause the release of cancer cells into the blood or LYMPH circulation is very high with testicular cancer because of the circulatory and lymphatic structures of the testicle. The urologist may consider biopsy when both testicles are involved or when a man has only one testicle. In such a circumstance the OPERATION begins as would an inguinal orchiectomy but the surgeon sends a tissue sample for the pathologist to examine and waits for the report of cancer or not cancer before proceeding. Otherwise laboratory analysis of the tumor occurs after removal of the testicle and its spermatic cord. The pathologist then identifies the type and stage of the cancer, which determines appropriate treatment options.

Treatment Options and Outlook

Surgery to remove the testicle containing the cancer is the first line of treatment. The operation of choice is radical inguinal ORCHIECTOMY, performed with the man under general ANESTHESIA. The surgeon makes an incision in the groin and pulls the testicle up from the scrotum to remove it, intact, along with its spermatic cord. The spermatic cord contains the blood and lymph vessels that supply the testicle; removing the entire testicular structure significantly reduces the risk for stray cancer cells entering the blood and lymph circulations to spread elsewhere in the body.

For seminomas or large tumors, the surgeon may also remove lymph nodes in the lower abdomen that are the path of lymph drainage from the spermatic cord (retroperitoneal LYMPH NODE dissection). Though a more extensive surgery, such an operation is very successful in preventing the spread of the cancer.

Most men then receive adjuvant (accompanying) treatment with RADIATION THERAPY or CHEMOTHERAPY, depending on the type and stage of the cancer. Tumors that contain only seminoma cells (pure seminoma) tend to stay contained longer and are very sensitive to radiation therapy. Tumors that contain nonseminoma cells tend to metastasize (spread) earlier and are more responsive to chemotherapy. Oncologists typically administer chemotherapy using combinations of drugs for several cycles (three or four) of treatment.

CHEMOTHERAPY AGENTS TO TREAT TESTICULAR CANCER

bleomycin	carboplatin
cisplatin	cyclophosphamide
etoposide	ifosfamide
vinblastine	

Testicular cancer is among the most treatable cancers. Testicular cancer detected and treated while it remains localized in one testicle (stage 0 or stage 1) has a current five-year survival rate of 99 percent; oncologists consider this a cure rate because the cancer rarely recurs. The RECURRENCE rate (likelihood for the cancer to return after treatment) is very low, though a man who has had testicular cancer has increased risk for cancer in the remaining testicle (usually a new cancer rather than a metastasis of the original cancer) or for other types of cancer.

Treatment for testicular cancer does not affect a man's sexuality though may affect his FERTILITY. Most people feel fatigued during cancer treatment, which often lowers LIBIDO (interest in sexual activity). However, most testicular cancer treatments do not affect a man's ability to obtain ERECTION, reach orgasm, or achieve EJACULATION. Extensive retroperitoneal lymph node dissection has a slight risk for NERVE damage that can result in RETROGRADE EJACULATION (in which SEMEN enters the BLADDER rather than exiting the PENIS during ejaculation). Many men retain fertility after testicular cancer, though doctors recommend sperm banking for men who may desire to father children because many factors influence fertility so it is not certain. A man may choose to have a testicular prosthesis implanted to restore the cosmetic appearance and feel of the scrotum.

Risk Factors and Preventive Measures

The most significant risk factor for testicular cancer is undescended testicle (CRYPTORCHIDISM), even after corrective treatment. Untreated cryptorchidism in which the testicle remains within the abdomen presents a very high risk as well as low potential for early detection of testicular cancer. Testicular atrophy, such as may occur after INFECTION with the MUMPS VIRUS, bacterial ORCHITIS, or SEXUALLY TRANSMITTED DISEASES (STDS), and family or personal history of testicular cancer also increase a man's risk for testicular cancer. Though there are no measures to prevent testicular cancer, monthly TSE is an effective means of early detection. Regular follow-up care, including blood tests to measure tumor markers and imaging procedures such as COMPUTED TOMOGRAPHY (CT) SCAN or POSITRON EMISSION TOMOGRAPHY (PET) SCAN, is important.

See also BREAST CANCER; CANCER TREATMENT OPTIONS AND DECISIONS; HORMONE-DRIVEN CANCERS; PROSTATE CANCER; SEXUAL HEALTH; STAGING AND GRADING OF CANCER; SURGERY FOR CANCER.

testicular self-examination A technique by which a man checks his TESTICLES for lumps, PAIN, and other abnormalities as a means of early detection of TESTICULAR CANCER and noncancerous conditions that may affect the testicles and a man's fertility, such as VARICOCELE and HYDROCELE. The primary purpose of TSE is to familiarize a man with the characteristics and anatomy of his testicles so he can detect changes that occur because it is these changes that may signal health conditions that require medical treatment. Though the main intent of TSE is early detection of testicular cancer, as mentioned, the technique also detects noncancerous conditions such as SPERMATOCELE, which can reduce fertility.

Health experts recommend TSE monthly, such as on the first day of every month, and suggest doing TSE in the shower when the SCROTUM is relaxed and lowered and the hands are soapy. TSE takes only a few minutes, following these steps:

1. Cup the testicles in one hand to support them.
2. Gently roll one testicle between the fingers, feeling for small lumps or unusual tenderness. The testicle should feel firm and smooth.
3. Use the fingers to feel the cordlike structure that runs from top to bottom, along the back of the testicle, the epididymis, exploring for hard lumps or areas of unusual tenderness. The epididymis is a tightly coiled structure that should feel somewhat lumpy or ropelike.
4. Use the fingers to feel the tubelike structure that runs from bottom to top along the side of the testicle, the VAS DEFERENS, checking for lumps or areas of unusual tenderness. The vas deferens should feel smooth and firm, and should move easily within the scrotum.
5. Repeat for the other testicle.

A doctor should promptly evaluate any changes or unusual findings such as lumps. It is normal for the testicles to be somewhat different in size and for one to hang lower than the other within the scrotum. Factors that increase a man's risk for developing testicular cancer include undescended testicle (CRYPTORCHISM), even after treatment to correct it, and family or personal history of testicular cancer. Testicular cancer is most common in men between the ages of 20 and 40, though can occur at any age. With early detection and treatment testicular cancer is highly treatable or curable, which is what makes TSE so important.

See also BREAST SELF-EXAMINATION (BSE); PROSTATE HEALTH; ROUTINE MEDICAL EXAMINATION; SEXUAL HEALTH.

testicular torsion A condition in which the spermatic cord twists within the SCROTUM, turning the testicle and jeopardizing its BLOOD supply. Testicular torsion is very painful and can result in loss of the testicle due to strangulation (cutting off the flow of blood to the testicle). Testicular torsion may occur as a result of injury or may occur spontaneously (without apparent cause) and is most common in boys between the ages of 8 and 14. Normally connective tissues firmly attach the epididymis to the SCROTUM; in testicular torsion this attachment either did not exist (congenital) or broke free with exertion or a blow to the TESTICLES.

Testicular torsion is a medical emergency that requires urgent treatment from a doctor.

The key symptoms of testicular torsion are PAIN, swelling, and discoloration (cyanosis) of the scrotum. Symptoms usually appear suddenly, though some boys or men have recurring symptoms over time. Because of the structure of the spermatic cord, testicular torsion most often affects the left testicle. Chronic symptoms suggest congenital detachment of the epididymis from the scrotum. The diagnostic path includes careful physical assessment of the testicles, usually by a urologist. ULTRASOUND (usually Doppler ultrasound) can confirm the diagnosis.

Treatment, when diagnosis comes within six to eight hours of the first symptoms, is emergency surgery to restore the testicle to its normal position and attach it to the scrotum (ORCHIOPEXY). The testicle cannot survive more than six to eight hours after symptoms emerge; after this time necrosis (death of the tissue) sets in and the only treatment is to remove the testicle (ORCHIECTOMY). With rapid and appropriate treatment the urologist can save the testicle about 80 percent of the time. However, testicular atrophy (wasting) and necrosis (tissue death) remain possible for up to six months after the surgery to remedy testicular torsion.

The longer the time between the onset of symptoms and surgery, the greater the likelihood for impaired FERTILITY even when the urologist can save the testicle. This is because the SPERM that escape into the tissues of the testicle establish or activate the IMMUNE RESPONSE, which produces antibodies to the man's own sperm that then attack the sperm as the testicles produce them.

See also EPIDIDYMITIS; GENITAL TRAUMA; HERNIA; ORCHITIS; SEXUAL HEALTH.

tubal ligation A surgical OPERATION to sever (cut) or tie off a woman's FALLOPIAN TUBES to prevent PREGNANCY. Tubal ligation is a form of permanent CONTRACEPTION, sometimes called tying the tubes or sterilization. There are two fallopian tubes, one leading from each ovary to the UTERUS. Cutting or cauterizing the fallopian tubes prevents the union of OVA, which travel from the OVARIES to the uterus, and SPERM, which travel from the uterus toward the ovaries. This blocks fertilization and prevents pregnancy.

Surgical Procedure

The most common method of tubal ligation is an abdominal operation usually performed as a laparoscopic procedure in an AMBULATORY SURGICAL FACILITY (outpatient or same-day surgery). The doctor may also perform tubal ligation as an OPEN SURGERY at the conclusion of a scheduled CESAREAN SECTION, provided the woman has given informed consent for the procedure.

The woman first receives ANESTHESIA, which may be general anesthesia (deep sleep) or regional anesthesia such as an epidural block. The surgeon then makes a single incision (called a single puncture technique) or several small incisions near the area of the navel (belly button) to insert the laparoscope and operating instruments. The incisions give access to the fallopian tubes. The surgeon places surgical clips or uses cautery to close the tubes. There may or may not be SKIN sutures, depending on the method the surgeon uses. The operation typically takes 35 to 45 minutes.

The woman spends one to three hours in the recovery room after the operation, until she emerges from the effect of the anesthesia. Most women go home within four to six hours of the operation. There is some abdominal discomfort for one to three days, for which the doctor will prescribe or recommend appropriate ANALGESIC MEDICATIONS. Full recovery may take two to three weeks, though many women can return to most normal activities within a few days. INFERTILITY is immediate.

Risks and Complications

As with any surgery, tubal ligation carries the risk for excessive bleeding, INFECTION, and reaction to the anesthesia. However, these complications are uncommon. Also possible though uncommon is PELVIC INFLAMMATORY DISEASE (PID), in which infection becomes widespread within the fallopian tubes and uterus and may also involve other abdominal structures. Rarely a fallopian tube may spontaneously reanastomose (reconnect), resulting in unexpected fertility usually detected through pregnancy.

Complications that may occur months to years after the operation include abdominal adhesions (the formation of restrictive SCAR tissue within the abdominal cavity) and ECTOPIC PREGNANCY, a life-

threatening circumstance that typically occurs when a tube partially reanastomoses but the fertilized egg cannot pass through the tube to the uterus and instead begins to grow in the fallopian tube or the abdominal cavity.

Outlook and Lifestyle Modifications

Tubal ligation has no effect on a woman's LIBIDO (sex drive), and in fact may increase a woman's interest in sexual activity because she no longer worries about unintended pregnancy. However, tubal ligation does not protect against SEXUALLY TRANSMITTED DISEASES (STDS) or HIV/AIDS.

The intent of tubal ligation is to establish permanent infertility (sterility), and a woman should consider tubal ligation to be permanent though it is sometimes possible to reverse a tubal ligation through a second surgery. The operation to reverse tubal ligation is usually major abdominal open surgery; its success depends on multiple factors, including the woman's current age and the age at which she had the tubal ligation and the skill of the surgeon.

See also CONCEPTION; FAMILY PLANNING; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; VASECTOMY.

Turner's syndrome A spontaneous (nonhereditary) chromosomal disorder in which there are abnormalities of the X CHROMOSOME, the SEX CHROMOSOME that establishes female gender, resulting in various anatomic and physiologic anomalies. These abnormalities may include only a single X chromosome (X chromosome deletion) instead of the normal pair of X chromosomes, or one complete and one fragmented or partial X chromosome. As well, the pattern may be mosaic, with some cells in the body carrying the normal paired X chromosome complement and others carrying the abnormality. Turner's syndrome affects only females.

Though symptoms of Turner's syndrome vary depending on the severity of the chromosomal abnormality, characteristic traits include very short stature and loss or lack of ovarian function. An unusually short neck with webbed SKIN, and a broad, shield-shaped chest may be prominent at birth to suggest the presence of Turner's syndrome though often the diagnosis comes later in childhood or early ADOLESCENCE when SECONDARY SEXUAL CHARACTERISTICS fail to develop. GENETIC TESTING (KARYOTYPE) confirms the diagnosis. Anomalies of the HEART (coarctation of the AORTA) and KIDNEYS (HORSESHOE KIDNEY) are also common. As adults, women who have Turner's syndrome have increased risk for type 2 DIABETES, HYPOTHYROIDISM (underactive THYROID GLAND function), HYPERTENSION (high BLOOD PRESSURE), and OSTEOPOROSIS.

HORMONE THERAPY with ESTROGENS and progestin from PUBERTY through midlife (to the age MENOPAUSE would normally occur, around 50) is the standard course of treatment for Turner's syndrome. This treatment causes relatively normal development of secondary sexual characteristics and sometimes of ovarian function to produce hormones, though the OVARIES do not produce normal OVA. In mosaic Turner's syndrome, the woman's ovaries may function until early adulthood. ASSISTED REPRODUCTIVE TECHNOLOGY (ART) techniques can make PREGNANCY possible. There are no measures to prevent Turner's syndrome.

See also CHROMOSOMAL DISORDERS; GENETIC DISORDERS; KLINEFELTER'S SYNDROME; MOSAICISM.

U

umbilical cord The entwinement of the two umbilical arteries, one umbilical VEIN, and nerves that extend from the PLACENTA to the developing FETUS during PREGNANCY. The length of the umbilical cord varies according to numerous factors. The flow of BLOOD through the umbilical arteries and vein holds the umbilical cord relatively rigid. A thick gelatinous coating, called Wharton's jelly, surrounds the umbilical cord to protect it as it floats in the AMNIOTIC FLUID.

The umbilical cord carries nourishment from the mother to the fetus and metabolic waste from the fetus to the mother via the blood circulation. The umbilical cord enters the fetus in the center of its abdomen. The umbilical arteries carry blood from the fetus to the placenta, which delivers oxygen and NUTRIENTS to the blood. The umbilical vein then carries the oxygenated blood back to the fetus.

The third stage of childbirth is delivery of the placenta, often called the afterbirth. When the woman delivers the umbilical cord the doctor or midwife clamps it in two places, cuts between the clamps, and seals the end attached to the baby with a plastic clip. Within two to three weeks the stump of the umbilical cord shrivels, hardens, and falls off. In its place remains the SCAR that forms to close off the umbilical portal into the infant's body, the umbilicus or navel (commonly called the belly button). The remnants of the umbilical arteries and umbilical vein become ligaments within the abdomen.

For further discussion of the umbilical cord within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also ARTERY; BLOOD STEM CELLS; NERVE.

uterine fibroids Benign (noncancerous) tumors of connective tissue and MUSCLE that grow from the walls of the UTERUS. Uterine fibroids, also called uterine leiomyomas or fibromyomas, may grow inward into the inner cavity of the uterus (submucosal fibroids), within the layers of the myometrium (muscular wall of the uterus), or outward from the myometrium into the abdominal cavity (subserosal fibroids). Pedunculated fibroids grow on stalks and can be submucosal or subserosal.

Uterine fibroids are very common. They may occur as isolated or clustered growths ranging in size from barely visible to the eye to as big as grapefruit. Uterine fibroids may cause symptoms when they press against other abdominal structures such as the BLADDER or RECTUM, when a pedunculated fibroid twists on its stalk, or when a fibroid dies and releases fluid and debris that irritates the surrounding tissues.

Symptoms and Diagnostic Path

Three fourths of women who have uterine fibroids have no symptoms; the doctor detects the fibroids during routine PELVIC EXAMINATION or ULTRASOUND performed for other reasons. When symptoms occur they often include

- low abdominal (pelvic) pressure or PAIN that often intensifies during MENSTRUATION
- heavy or prolonged menstrual bleeding
- bleeding between menstrual periods
- CONSTIPATION or DIARRHEA
- pain in the lower back or the upper legs

Uterine fibroids may also create FERTILITY problems when they are large enough or when they

grow in positions, especially near the openings of the FALLOPIAN TUBES, that prevent the implantation of a fertilized egg (ZYGOTE). Large fibroids may interfere with the growth of the FETUS, causing spontaneous ABORTION (miscarriage).

The diagnostic path includes pelvic examination and imaging procedures such as ultrasound, COMPUTED TOMOGRAPHY (CT) SCAN, or MAGNETIC RESONANCE IMAGING (MRI). The doctor may also perform HYSTEROSCOPY to view the inner uterus or laparoscopy to view the abdominal cavity. These procedures, performed with ANESTHESIA, also allow the doctor to also take small samples of the growths for further laboratory analysis.

Treatment Options and Outlook

Uterine fibroids that do not cause symptoms do not require treatment. Often, uterine fibroids shrink on their own with MENOPAUSE and then cease to cause symptoms. Medical treatments include

- NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which effectively relieve the discomfort of uterine fibroids when symptoms are mild
- hormones such as GONADOTROPIN-RELEASING HORMONE (GNRH) agonists (such as leuprolide) and ANDROGENS (such as Danocrine) that alter the hormonal balance in the body, causing the fibroids to shrink
- oral contraceptives (birth control pills), particularly progestin-only products, which may reduce symptoms with fewer risks and side effects than other HORMONE therapies

These drugs all have significant side effects and affect fertility during the course of treatment. Though these medications are effective, a woman can take them for only a limited time and the fibroids rapidly return when she stops taking the medication.

Surgical treatment options include removal of the fibroids (myomectomy), which preserves fertility, and removal of the uterus (HYSTERECTOMY), which ends fertility. Uterine fibroid embolization (UFE) is an option for some fibroids. For this procedure an interventional radiologist injects sterile polyvinyl alcohol (PVA) particles through a catheter inserted into the femoral ARTERY in the groin and threaded into the arteries that supply the fibroids. The particles block the arteries, cutting off the fibroid's BLOOD supply and causing it to die.

Risk Factors and Preventive Measures

Uterine fibroids are most common in women who are between ages 30 and 40. Though the cells that form uterine fibroids have more estrogen receptors (molecules that accept, or bind with, ESTROGENS) than normal myometrial cells and most fibroids recede with menopause, the correlation between estrogen and fibroids remains unclear. There are no measures to prevent uterine fibroids from developing.

See also ADENOMYOSIS; ENDOMETRIOSIS; SURGERY BENEFIT AND RISK ASSESSMENT.

uterine prolapse A circumstance in which the ligaments and muscles that support the UTERUS within the abdomen weaken, allowing the uterus to sag into the VAGINA. The weakness generally occurs as a consequence of multiple pregnancies that stress them or traumatic CHILDBIRTH that causes damage to them. OBESITY increases the risk for uterine prolapse. Less commonly, uterine prolapse may develop in a woman who has long-term chronic COUGH such as may occur with chronic BRONCHITIS or CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD).

The symptoms of uterine prolapse may include

- sensation of heaviness or pressure in the lower pelvis
- PAIN during SEXUAL INTERCOURSE
- lower BACK PAIN

Depending on the severity of the prolapse, the uterus and cervix may protrude into the vagina or through the entrance of the vagina (vaginal introitus). The diagnostic path includes PELVIC EXAMINATION, which is typically sufficient for the doctor to diagnose uterine prolapse.

Treatment for mild to moderate uterine prolapse is most often a vaginal pessary, a fitted device the woman inserts into her vagina to hold the uterus in position. Treatment for moderate to severe uterine prolapse is surgery either to repair the muscles and ligaments (sacral colpopexy) or to

remove the uterus (HYSTERECTOMY). Surgery provides permanent correction, though in some women the damage to the pelvic structures may later experience vaginal prolapse (sagging of the vaginal walls).

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; CYSTOCELE; LIGAMENT; MUSCLE; PREGNANCY; RECTOCELE; SURGERY BENEFIT AND RISK ASSESSMENT.

uterus The hollow muscular organ that supports and contains a PREGNANCY. Eight ligaments—one anterior, one posterior, two round, two broad (also called lateral), and two uterosacral—suspend the pear-shaped uterus in the lower central abdomen (pelvis), with the narrow end of the uterus angled somewhat downward. This suspension system allows the uterus, also called the womb, to expand during pregnancy. The FALLOPIAN TUBES join the uterus, one on each side of the wide upper section called the fundus. The fundus angles forward such that the uterus lies above the urinary BLADDER.

The lower section of the uterus is the CERVIX, a thick neck of muscular tissue that joins the uterus with the VAGINA, the passage to the outside of the body. In its nonpregnant state the uterus is about three inches long and an inch thick; in PREGNANCY the uterus expands to become nearly 10 times as large as its nonpregnant size. Within four to six weeks after CHILDBIRTH the uterus returns to nearly its prepregnant size. The uterus has two layers of structure: the outer myometrium and the inner endometrium.

The surgical OPERATION to remove the uterus is HYSTERECTOMY, which may be treatment for ENDOMETRIAL CANCER, severe ENDOMETRIOSIS or UTERINE FIBROIDS, or DYSFUNCTIONAL UTERINE BLEEDING (DUB).

The myometrium The myometrium is three layers of strong, smooth (involuntary) MUSCLE. The fibers of the innermost layer form two circular patterns that emanate from the fallopian tubes and extend to the cervix. The fibers of the middle layer occur in random patterns that run lengthwise, widthwise, and diagonally. These fibers primarily support the network of BLOOD vessels that nourish the myometrium. The outermost layer's fibers wrap diagonally (transversely) around the uterus.

The myometrium grows during pregnancy to accommodate the growing and enlarging FETUS. Through mechanisms doctors do not fully understand, the myometrium begins rhythmic and increasingly intense waves of contractions, synchronized across the three layers of muscle, that ultimately result in childbirth. The contractions stretch and thin (efface) the cervix and then push the fetus through the cervix, into the vagina, and out of the body.

The endometrium The inner structure of the uterus is the endometrium, a membranous tissue that contains abundant blood vessels and glands. The endometrium responds to the monthly hormonal cycle of estrogen and PROGESTERONE peaks and troughs, thickening when blood levels of ESTROGENS rise—a preparation for pregnancy—and sloughing when estrogen drops and progesterone rises—MENSTRUATION. When these hormonal cycles cease with MENOPAUSE, the endometrium enters a state of atrophy, in which it remains for the rest of the woman's life.

HEALTH CONDITIONS THAT CAN AFFECT THE UTERUS

ADENOMYOSIS	DYSFUNCTIONAL UTERINE BLEEDING (DUB)
ENDOMETRIAL CANCER	ENDOMETRIAL HYPERPLASIA
ENDOMETRIOSIS	PELVIC INFLAMMATORY DISEASE (PID)
PREGNANCY	UTERINE FIBROIDS

For further discussion of the uterus within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also HYSTEROSCOPY; OVARIES; SEXUAL HEALTH.

V–Z

VACTERL The acronym for a constellation of BIRTH DEFECTS that tend to occur in coincidence with each other. Doctors consider a baby who has three or more of the defects to have the VACTERL association, and will examine the baby closely for the other defects in the constellation. These defects include

- V: vertebral (spinal) anomalies
- A: ANAL ATRESIA (also called imperforate ANUS)
- C: cardiac (HEART) anomalies
- T/E: tracheoesophageal fistula (may also occur as tracheal fistula and ESOPHAGEAL ATRESIA)
- R: renal (kidney) anomalies
- L: limb anomalies

Occurring often enough that some doctors believe it, too, is part of the constellation, is a single-ARTERY UMBILICAL CORD (the normal umbilical cord has two arteries), which sometimes appears in the acronym as a final *S* (VACTERLS). VACTERL occurs sporadically (in a nonhereditary pattern); researchers do not know what causes it, nor do they understand the connections among the various defects. Some of the birth defects can be life threatening, such as the HEART malformation tetralogy of Fallot (a complex of four serious heart defects). Treatment, often surgery, attempts to correct the congenital anomalies.

See also CONGENITAL ANOMALY; CONGENITAL HEART DISEASE.

vagina The muscular passageway between the CERVIX and the VULVA (outside of the body). The vagina serves as the portal through which the menstrual flow leaves the body with MENSTRUATION, the erect PENIS enters during SEXUAL INTERCOURSE, and the FETUS passes during CHILDBIRTH.

The outer structures of the vagina are strong muscles that have the ability to vary the inner diameter of the vagina from its normal state in which the vaginal walls touch each other to four or five inches to accommodate the birth of a child. Deep folds of mucous membrane (the vaginal mucosa) line the vagina. The folds, called rugae, give the vagina its ability to expand. The vaginal muscles also relax to extend the depth (length) of the vagina, facilitating SEXUAL INTERCOURSE.

The vaginal tissue near the opening of the vagina (the vaginal introitus) has an abundance of sensory NERVE endings though the rest of the vaginal mucosa has few sensory nerve endings. A small ring of vaginal mucosa, called the hymen, extends partially across the opening of the vagina. The degree to which the hymen restricts access to the vagina varies widely among women. Though conventional wisdom purports that penetration of the erect penis with a woman's first experience of sexual intercourse tears or ruptures the hymen, this may or may not be the case. A hymen that does not extend very far across the vaginal opening may not impede the entry of the erect penis. The hymen may also rupture or tear as a result of other factors such as insertion of tampons or activities such as horseback riding.

The Bartholin's glands and Skene's ducts near the entrance to the vagina and the nabothian glands (cervical glands) that cover the cervix provide secretions to moisten and lubricate the interior of the vagina. These secretions diminish with the loss of ESTROGENS that characterizes MENOPAUSE. As a result the vaginal mucosa becomes thin and fragile and the vagina less flexible after menopause.

HEALTH CONDITIONS THAT CAN AFFECT THE VAGINA

CANDIDIASIS (vaginal yeast INFECTION)	CHLAMYDIA
Escherichia coli INFECTION	GENITAL HERPES
GENITAL TRAUMA	GONORRHEA
HUMAN PAPILLOMAVIRUS (HPV)	SEXUAL ASSAULT
vaginal cancer	VAGINITIS

For further discussion of the vagina within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; BARTHOLIN'S CYST; COLPOSCOPY; MENSTRUAL CYCLE; NABOTHIAN CYST; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASES (STDS).

vaginitis INFLAMMATION of the VAGINA that may occur as a result of irritation or INFECTION. Common causes of irritation-based vaginitis include douches, feminine hygiene products, spermicides, bubble bath, and soaps. Common causes of infection-based vaginitis include CANDIDIASIS (yeast infection) and SEXUALLY TRANSMITTED DISEASES (STDS) such as CHLAMYDIA and TRICHOMONIASIS. Viruses that may cause vaginitis include HERPES SIMPLEX 2 (HSV-2), which causes GENITAL HERPES, and HUMAN PAPILLOMAVIRUS (HPV), which may cause clusters of wartlike growths. Other forms of vaginitis are bacterial (called gardnerella) and atrophic (which may occur after menopause).

Symptoms and Diagnostic Path

The symptoms of vaginitis typically include itching, burning, soreness, or other discomfort. When the cause is infection there may be a discharge or unusual odor. The diagnostic path includes discussion of sexual activity and any history of STDs, PELVIC EXAMINATION with PAP TEST, and laboratory examination or culture of any discharge to check for infection.

Treatment Options and Outlook

Treatment depends on the identified cause of the vaginitis and may include ANTIBIOTIC MEDICATIONS for bacterial infection (including STDs) or ANTIFUNGAL MEDICATIONS for yeast infection. When the cause is irritation, removing exposure to the source (such as a douche solution or spermicide) allows the vaginal tissues to heal. The doctor may prescribe topical CORTICOSTEROID MEDICATIONS to relieve symptoms. Tepid baths in water containing baking soda are often soothing. Wearing loose-fitting cotton underwear and avoiding pantyhose are other helpful measures. Most vaginitis improves rapidly with appropriate treatment.

Risk Factors and Preventive Measures

Vaginitis is very common in women, particularly women who are sexually active. SEXUAL INTERCOURSE, particularly with multiple sex partners or unprotected (without a barrier such as a condom), increases the risk for vaginitis. Women who use intrauterine devices (IUDs) for CONTRACEPTION also have increased risk for vaginitis as well as PELVIC INFLAMMATORY DISEASE (PID). Vaginitis is uncommon in prepubertal girls (girls who have not yet begun to menstruate) though may result from *ESCHERICHIA COLI* INFECTION as a consequence of poor toileting hygiene. Preventive measures include minimizing exposure to potential irritants and wearing clothing that allows some airflow between the fabric and the external GENITALIA.

See also PERSONAL HYGIENE; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

varicocele A VARICOSE VEIN in the testicle. Varicose veins are dilated, twisted, and often nonfunctioning veins that develop for numerous reasons. Varicocele affects the BLOOD flow that leaves the TESTICLES. Blood that accumulates in the testicles can raise the temperature within the SCROTUM high enough to interfere with proper SPERM formation (spermatogenesis) and maturation, resulting in INFERTILITY. A man may notice a varicocele as a soft bulge in his testicle that becomes more prominent when bearing down. Varicocele is more common in the left testicle because of the structure of the veins. The doctor can detect varicocele on palpating the testicles; Doppler ULTRASOUND, which shows the flow of blood, confirms the diagnosis.

Treatment is surgery to repair the varicocele. The OPERATION is an AMBULATORY SURGERY (the man goes home the same day). The man may receive general or regional ANESTHESIA. The most common operative technique involves a small incision made into the lower portion of the groin through which the surgeon can reach and repair the varicocele. HEALING is rapid and most men return to

regular activities, including sexual activity, within two weeks. When varicocele is the cause of infertility, FERTILITY usually returns when the surgical wound heals.

See also SPERMATOCELE; SURGERY BENEFIT AND RISK ASSESSMENT.

vas deferens A narrow tube that carries SPERM from the epididymis to the ejaculatory duct during ORGASM and EJACULATION. One vas deferens, also called a ductus deferens, arises from each testicle. The smooth-MUSCLE walls of the vas deferens contract and relax in wavelike movements to propel sperm from the testicle to mix with seminal fluid, which then carries the fluid (SEMEN) from the PENIS during ejaculation.

For further discussion of the vas deferens within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also FERTILITY; TESTICLES; VASECTOMY.

vasectomy A surgical OPERATION to sever (cut) the VAS DEFERENS, the narrow tubes that carry SPERM from a man's TESTICLES to the ejaculatory ducts where the sperm mixes with seminal fluid in preparation for EJACULATION (ejection from the PENIS during ORGASM). One vas deferens extends from each testicle, running very close beneath the surface of the SKIN of the SCROTUM.

Surgical Procedure

There are two methods for performing vasectomy, both of which are outpatient procedures usually done in the doctor's office. Each begins with the doctor injecting local ANESTHESIA into the scrotum to numb the area. For conventional vasectomy the doctor then makes two small incisions, one on each side of the scrotum, or a single incision at the base of the scrotum. Each vas deferens is accessible through the incision. The doctor cuts each vas deferens, removes a small segment to separate the ends, and sutures (stitches) the ends closed. The doctor then places several small, dissolving sutures to close the incisions in the scrotum.

For the nonsurgical or no scalpel vasectomy, the doctor locates and clamps the vas deferens through the skin of the scrotum using a special instrument called a ringed extracutaneous vas clamp. The clamp closes in a small circle; each tip is sharp. When closed the clamp makes a tiny puncture in the scrotum and pulls the vas deferens through the surface. The doctor cuts the exposed vas deferens, ties or cauterizes the ends, and tucks the sealed ends back inside the scrotum. The puncture heals without sutures. The doctor repeats the procedure on the other side.

Risks and Complications

Some swelling and discomfort is normal during the first 24 to 48 hours after the vasectomy. Ice to the scrotum and one of the NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) such as ibuprofen help relieve INFLAMMATION and PAIN. Wearing tight-fitting briefs or an athletic supporter for a few days gives additional support to the scrotum to minimize discomfort. Excessive bleeding and INFECTION are uncommon though can occur, as with any surgical operation. Some men experience HEMATOMA (collection of BLOOD within the scrotum) and GRANULOMA (SCAR tissue formation) after vasectomy. Most hematomas reabsorb within a week. Granulomas develop in reaction to sperm that leak into the tissues within the scrotum from the cut end of the vas deferens. Though granulomas are not harmful, they may remain tender or even painful for several weeks to several months.

Sperm may remain in the seminal ducts and other structures for quite some time, so a vasectomy is not effective immediately. A man must have two negative sperm counts one to two months after the vasectomy (or after 10 to 20 ejaculations) before he can consider himself infertile. It is essential to use an alternative method of CONTRACEPTION during this time. Because reanastomosis (also called recanalization) may occur years to decades after vasectomy, a man who has had a vasectomy should have periodic sperm counts throughout life to confirm that he remains infertile.

Outlook and Lifestyle Modifications

Vasectomy renders a man permanently infertile (sterile) by blocking the route by which sperm travel out of the testicles. Spermatogenesis (production of new sperm cells) continues; the body

eventually reabsorbs the sperm. Vasectomy does not alter a man's sexual desire or erectile function (ability to have an ERECTION). The ejaculate contains about the same amount of SEMEN as before vasectomy; the semen does not contain sperm, which slightly reduces its volume. There is a very slight risk for spontaneous reanastomosis (reconnection of the cut ends of the vas deferens) that can result in unexpected FERTILITY. Surgery to reverse vasectomy is sometimes possible to restore fertility, though multiple variables affect its success. Men should consider the loss of fertility with vasectomy to be permanent. Vasectomy does not provide protection against infection with SEXUALLY TRANSMITTED DISEASES (STDS) or HIV/AIDS.

See also FAMILY PLANNING; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SURGERY BENEFIT AND RISK ASSESSMENT; TUBAL LIGATION.

VBAC Vaginal birth after CESAREAN SECTION. In cesarean section, the obstetrician makes a surgical incision through the wall of the UTERUS to deliver the baby, then sutures (stitches) the incision closed. The SCAR that forms when the surgical wound heals is somewhat weaker than the surrounding MUSCLE of the uterus. When the incision is low and horizontal (transverse) in the uterus this slight weakness has little consequence. If the uterine incision runs vertically, however, there is an increased risk that the wall of the uterus could rupture along the scar during the intense contractions of labor and delivery. Uterine rupture is life threatening for the woman and the baby.

The obstetrician attempts to assess the likelihood of uterine rupture as the woman's PREGNANCY becomes advanced. The risk for uterine rupture is high enough with a vertical uterine scar that most obstetricians strongly discourage the woman from attempting vaginal delivery with subsequent pregnancies. If the obstetrician believes the risk for uterine rupture is low, which is usually the case with the low horizontal scar, VBAC is of little additional risk for the woman. Other factors that may influence the decision between a woman and her obstetrician about VBAC include the reason for the previous cesarean section and the woman's overall health status in her current pregnancy. About half of women who have cesarean deliveries are able to have vaginal deliveries in subsequent pregnancies.

See also CHILDBIRTH; PRENATAL CARE.

vulva See GENITALIA.

vulvodynia Chronic and sometimes severe vulvar PAIN a woman experiences. Though many women who have vulvodynia have had chronic or recurrent VAGINITIS (vaginal INFECTION), the connection between vaginitis and vulvodynia is unclear and only a small percentage of women who have vaginitis develop vulvodynia. There are few other discernible circumstances that could account for the symptoms of vulvodynia; doctors most often consider vulvodynia a CHRONIC PAIN syndrome.

The symptoms of vulvodynia often come on suddenly and may include

- intense burning, stinging, or itching of the vulva (labia, CLITORIS, and opening to the VAGINA)
- discomfort and soreness when sitting or walking
- PAIN during SEXUAL INTERCOURSE (dyspareunia)

The diagnostic path includes a thorough PELVIC EXAMINATION with cultures for yeast INFECTION (CANDIDIASIS) and SEXUALLY TRANSMITTED DISEASES (STDS) such as GONORRHEA and CHLAMYDIA. In vulvodynia, such test results are negative and the pelvic examination is normal. Treatment options include medications such as ANTIHISTAMINE MEDICATIONS, which lessen itching, and tricyclic ANTIDEPRESSANT MEDICATIONS, which act to block NERVE impulses related to pain. Other medications sometimes helpful for the pain of vulvodynia include certain antiseizure medications and topical CORTICOSTEROID MEDICATIONS. Other methods of pain relief that some women find helpful include cold compresses to the vulva, BIOFEEDBACK, ACUPUNCTURE.

Vulvodynia may persist for several months; rarely, symptoms may continue for more than a year. Eliminating any underlying causes for symptoms generally speeds recovery from vulvodynia as well. Relaxation techniques and compassionate communication between the woman and her sexual partner help with the emotional and sexual aspects of vulvodynia.

See also ALTERNATIVE METHODS FOR PAIN RELIEF; ANALGESIC MEDICATIONS; MALDYNIA; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

zygote The cell that results when a spermatozoon (SPERM cell) penetrates an ovum (egg cell) during fertilization. Each GAMETE (sperm and ovum) is a haploid cell; it contains one half the genetic material necessary to support life. The zygote is a diploid cell; it contains all the DNA necessary to create a new life. Fertilization typically takes place in the fallopian tube. The zygote grows and divides as it makes its way through the fallopian tube to the UTERUS, a journey of about five days. When it reaches the uterus the zygote implants into the endometrium, the thick, BLOOD-rich lining of the uterus. By the time implantation is complete the zygote has become a two-layered structure called a blastocyst.

For further discussion of the zygote within the context of the structures and functions of reproduction and sexuality, please see the overview section "The Reproductive System."

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); CELL STRUCTURE AND FUNCTION; EMBRYO; FALLOPIAN TUBE; FETUS; OVA.

PSYCHIATRIC DISORDERS AND PSYCHOLOGIC CONDITIONS

Psychiatry and psychology are disciplines within the practice of health care that deal with mental illness. Health-care professionals who provide care for people who have mental illnesses include psychiatrists, who are physicians (MDs or DOs); psychologists (PhDs); master's level therapists such as counselors (sometimes also called psychologists); social workers; and clinical registered nurse practitioners (CNRPs) who specialize in mental health. In the United States licensing requirements and practice limitations for mental health practitioners vary among states, though in all states only psychiatrists may prescribe medications.

This section, "Psychiatric Disorders and Psychologic Conditions," presents an overview discussion of mental health and mental illness and includes entries about psychiatric disorders, psychologic conditions, and their treatments. The section "The Nervous System" contains overview discussion and comprehensive entries about conditions that affect cognition, memory, and thought processes that arise from disease or injury to BRAIN structures that alters brain function.

Finding the Line between Mental Health and Mental Illness

Psychiatric disorders and psychologic conditions are those that doctors generally define as illnesses that arise from disrupted thought processes and their corresponding behaviors. However, the causes of mental illness remain poorly understood. Most psychiatric disorders reflect a mix of biochemical, behavioral, and genetic components. About 80 percent of people who have BIPOLAR DISORDER, for example, have other family members who have either bipolar disorder or clinical DEPRESSION that requires treatment.

The diagnosis of mental illness is often a significant challenge. One issue is that many of the symptoms that characterize mental illness are thoughts, feelings, and behaviors that everyone experiences to certain degree. However, in many situations it is less the symptoms themselves and more the level of dysfunction the symptoms cause in the person's life that defines the line between mental health and mental illness.

For example, a person may sometimes engage in speaking as though in conversation with another person when no one else is in fact present or talking, but knows the dialogue is a process of thinking aloud and can willingly start and stop the behavior. The behavior may appear amusing or quirky to others but does not interfere with the person's ability to interact with other people and to function in the world and thus in itself does not constitute mental illness.

It is a different picture when a person engages in dialogue with voices no one else can hear, but believes the voices are real and thus cannot control his or her interactions with them. In such a situation the person may believe the voices provide instruction or guidance, and behaves as though following directions the voices give. The messages from the voices may be nonsensical, confusing, demanding, or demeaning to the person and characteristically interfere with the person's ability to function in the world. This behavior represents a clear break with reality and interferes with the person's ability to function in the world and thus constitutes mental illness.

The Diagnostic Path for Psychiatric Disorders and Psychologic Conditions

The diagnostic path for mental illness begins with the elimination of potential physical or physio-

logic causes for symptoms. Loss of inhibition, for example, may occur as a consequence of STROKE, ALZHEIMER'S DISEASE, or BRAIN TUMOR. There is a high correlation between untreated HYPOTHYROIDISM and bipolar disorder. When the doctor can eliminate physical causes, the emphasis shifts to psychologic evaluation to identify the disorder. Because many psychologic conditions and psychiatric disorders have overlapping symptoms, distinguishing among them is often a challenge.

In the United States most providers and insurance companies follow the diagnostic criteria and treatment algorithms detailed in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, commonly called the DSM. The current version of the DSM includes a Roman numeral in the title to differentiate it from previous versions; for example, DSM-IV indicates the fourth version. Though other diagnostic criteria and treatment methods are available and valid, the DSM reflects the conventional perspective and is widely accepted as the standard.

Treatment and Outlook for Psychiatric Disorders and Psychologic Conditions

The mainstays of treatment for psychiatric disorders and psychologic conditions are medications and therapy. As is the case with numerous physical health conditions, treatment often cannot cure the condition and so aims to instead manage symptoms. A person who has HYPERTENSION (high BLOOD PRESSURE) often needs lifelong antihypertensive medications and lifestyle modifications to support cardiovascular health (such as WEIGHT LOSS AND WEIGHT MANAGEMENT and nutritious EATING HABITS). This therapeutic approach regulates the body's functions in regard to BLOOD pressure though does not end the underlying factors causing the hypertension. Likewise, a person who has bipolar disorder may need lifelong mood stabilizing medications in combination with PSYCHOTHERAPY and lifestyle measures to limit exacerbations of symptoms.

Combinations of different types of medications are common because the boundaries of many mental disorders are not clear cut and the biochemical functions that underlie them are similar. Both depression and anxiety often respond to treatment with selective serotonin reuptake inhibitor (SSRI) antidepressants, for example, even though they present different symptoms. As well, some mental disorders, such as SCHIZOPHRENIA and bipolar disorder, have multiple components that often require different types of medication to moderate symptoms.

Because most psychiatric disorders and psychologic conditions result from multiple factors, including genetic and physiologic, there is usually no way to prevent them from occurring. Many conditions respond to treatment to manage symptoms so that the condition has a negligible effect on the person's QUALITY OF LIFE. Some short-term, reactive, or narrowly defined conditions such as BRIEF REACTIVE PSYCHOSIS, POST-TRAUMATIC STRESS DISORDER (PTSD), or certain phobias are curable with appropriate treatment.

A

acute stress disorder A dissociative state (mental framework that creates emotional and psychologic distance from the trauma) that occurs in reaction to a traumatic event. Symptoms often begin within hours of the event and may last for a few hours to a few days. The person may speak about the trauma in the third person as though it happened to someone else, may act as though the trauma did not occur, may be unable to remember the event (dissociative amnesia), or may have an apparent lack of emotional response regarding the event. The person may appear dazed and "out of it" or have acute and severe symptoms of DEPRESSION or anxiety. Flashbacks and dreams in which he or she relives the traumatic event are common. Normal, everyday circumstances may also trigger flashbacks.

Diagnosis is usually straightforward because the connection between the traumatic event and the symptoms is clear. Treatment may include supportive therapy along with short-term ANTIANXIETY MEDICATIONS or ANTIDEPRESSANT MEDICATIONS. Rarely, the symptoms continue for as long as several weeks, though psychiatrists are more likely to diagnose continuing symptoms as POST-TRAUMATIC STRESS DISORDER (PTSD).

See also BRIEF REACTIVE PSYCHOSIS; CHILD ABUSE; DOMESTIC VIOLENCE; ELDER ABUSE; GENERAL ANXIETY DISORDER (GAD); GRIEF; SEXUAL ASSAULT; STRESS AND STRESS MANAGEMENT; VIOLENCE.

antianxiety medications Medications to relieve symptoms of anxiety disorders. About 15 percent of adults in the United States have anxiety disorders for which they take antianxiety medications. There are two types of antianxiety medications in use today, the BENZODIAZEPINES and buspirone. As well, many of the ANTIDEPRESSANT MEDICATIONS, notably the selective serotonin reuptake inhibitors (SSRIs), also successfully relieve the anxiety symptoms.

The first medications to treat anxiety were barbiturates, which produce a fairly substantial level of sedation, particularly at the onset of treatment. Barbiturates, commonly called tranquilizers, are also highly addictive and have significant risk for death due to OVERDOSE. For these reasons doctors no longer prescribe barbiturates to treat anxiety. Meprobamate was the first medication developed specifically to treat anxiety disorders. Though not chemically a barbiturate, it has many of the same actions and side effects. Doctors today occasionally prescribe meprobamate to treat anxiety in people who cannot take or do not respond to other antianxiety medications or who have coexisting psychotic disorders.

Doctors sometimes prescribe a beta blocker medication, commonly propanolol, to relieve episodic symptoms that arise specifically from performance anxiety. Beta blockers inhibit the flow of EPINEPHRINE, which prevents symptoms such as rapid HEART RATE and increased sweating. Beta blockers are not appropriate for other types of anxiety, however, because they do not affect the neurotransmitters primarily responsible for anxiety symptoms.

Benzodiazepines The first generation of benzodiazepines, chlordiazepoxide (Librium) and diazepam (Valium), came into use in the early 1960s and quickly replaced both barbiturates and meprobamate in the treatment of anxiety disorders. The benzodiazepines produce rapid relief from symptoms, some of them within hours of the first DOSE. This characteristic makes benzodiazepines useful for immediate or episodic relief of anxiety symptoms. There are now nearly a dozen

benzodiazepine drugs on the market; they differ primarily in the extent of sedation they cause, the onset of action, and the length of time they are active in the body.

BENZODIAZEPINE ANTIANXIETY MEDICATIONS	
alprazolam	chlordiazepoxide
clonazepam	clorazepate
diazepam	flurazepam
halazepam	lorazepam
oxazepam	prazepam
temazepam	

Buspirone is a unique DRUG that does not belong to existing chemical classification and is primarily effective as treatment for moderate to moderately severe GENERALIZED ANXIETY DISORDER (GAD). Buspirone does not appear to be particularly effective for treating PANIC DISORDER, OBSESSIVE–COMPULSIVE DISORDER (OCD), or PHOBIA. The person must take buspirone regularly for two to three weeks before experiencing relief from anxiety symptoms.

How These Medications Work

The benzodiazepines work by binding with neuroreceptors on BRAIN neurons for gamma-aminobutyric acid (GABA), a NEUROTRANSMITTER that inhibits electrical activity. This binding extends GABA's availability, intensifying its inhibiting actions and consequently inducing emotional and neurologic calmness and, at high enough doses, sedation. The mechanisms of buspirone are unknown, though it does not act on GABA or produce sedation at any dose.

Therapeutic Applications

Doctors commonly prescribe antianxiety medications to treat mental disorders such as GAD, ACUTE STRESS DISORDER, panic disorder, POST-TRAUMATIC STRESS DISORDER (PTSD), phobias, and OCD. Doctors may also prescribe antianxiety medications, sometimes called anxiolytics, to relieve short-term anxiety related to ALCOHOL DETOXIFICATION as well as to provide a sense of calm before minor dental and medical procedures. Many of the benzodiazepines have other clinical applications, such as MUSCLE relaxants and hypnotics (drugs that provide conscious sedation). Doctors sometimes prescribe benzodiazepines to treat clonic-tonic seizures in SEIZURE DISORDERS and spasticity in disorders such as CEREBRAL PALSY and SPINAL CORD INJURY.

Risks and Side Effects

Key risks with long-term benzodiazepines are dependence and tolerance. The longer a person takes a benzodiazepine medication the more accustomed the brain becomes to it. Achieving consistent effects over time often means gradually increasing the dosage. Suddenly stopping a benzodiazepine medication after taking it for longer than six weeks may result in a withdrawal syndrome with various discomforts, including agitation, irritability, HEADACHE, and sleep disturbances. Doctors recommend tapering the dose over two or three weeks rather than abruptly stopping a benzodiazepine. Buspirone does not cause dependency or tolerance, though it also can cause unpleasant symptoms when stopped suddenly.

See also DEPRESSION; MUSCLE RELAXANT MEDICATIONS; VALERIAN.

antidepressant medications Medications primarily to treat depression. About 25 percent of adults in the United States have depression and more than 80 percent of them take antidepressant medications. There are several classifications, also called generations, of antidepressant medications. The drugs in each classification work by somewhat different mechanisms from those in other classifications.

Researchers have linked antidepressant use in children and teenagers with increased risk for suicide. The US Food and Drug Administration (FDA) requires warnings on the labels of drugs for which this risk is significant and cautions parents to closely observe children who take antidepressant medications for signs of increased DEPRESSION or expressions of interest in suicide.

Monoamine oxidase inhibitors (MAOIs) Researchers developed the first antidepressant medications, the MAOIs, in the early 1950s. This class of antidepressant works by a somewhat dif-

ferent mechanism from subsequent classes in that it blocks the function of an enzyme (monoamine oxidase, or MAO) to indirectly extend the availability of the neurotransmitters DOPAMINE, NOREPINEPHRINE, and serotonin. Unfortunately, the body requires MAO to metabolize tyramines, proteins that occur naturally in certain foods. Unmetabolized tyramines affect cardiovascular function and can cause rapid, extreme elevations in BLOOD PRESSURE, which presents a significant risk for STROKE. People taking MAOIs must avoid eating foods high in tyramines, such as smoked meats, cheeses, wines, and fermented or pickled foods. Because the risk for potentially fatal HYPERTENSION (high blood pressure) is so high, doctors prescribe MAOIs primarily as a final treatment option when other antidepressant medications do not improve symptoms.

MONOAMINE OXIDASE INHIBITOR (MAOI) ANTIDEPRESSANTS

isocarboxazid	phenelzine
tranylcypromine	

Tricyclics The tricyclic class of antidepressants, so-called because of their three-ringed molecular structure, entered the market in the early 1960s as a welcome alternative to MAOIs. This second generation of antidepressants became the most widely prescribed antidepressant medications for 30 years, leading treatment protocols until selective serotonin reuptake inhibitors (SSRIs) supplanted them in the 1980s. Tricyclics, also called TCAs, appear to selectively suppress serotonin and norepinephrine reuptake, though the precise mechanisms by which they do so remain unknown.

Doctors may prescribe tricyclic antidepressants to treat other health conditions, notably ENURESIS (bedwetting), OBSESSIVE–COMPULSIVE DISORDER (OCD), CHRONIC FATIGUE SYNDROME, and some CHRONIC PAIN syndromes such as FIBROMYALGIA and chronic regional PAIN syndrome. Though an improvement over MAOIs, with their multitude of side effects, the tricyclic antidepressants have some significant side effects of their own, most bothersome among them being drowsiness, dry MOUTH, CONSTIPATION, and SEXUAL DYSFUNCTION. Doctors now tend to prescribe tricyclics as second-line treatment for depression that does not improve with SSRIs.

TRICYCLIC ANTIDEPRESSANTS

amitriptyline	clomipramine
desipramine	doxepin
imipramine	nortriptyline
protriptyline	trimipramine

Selective serotonin reuptake inhibitors (SSRIs) The SSRIs block reuptake of only serotonin, eliminating or diminishing many of the side effects attributable to inhibited reuptake of norepinephrine, which is a feature of MAOIs and tricyclics. Doctors now prescribe SSRIs as the first line of medication treatment to treat moderate depression in most people. SSRIs are also effective in treating the EATING DISORDERS anorexia nervosa and bulimia. At lower doses than doctors typically prescribe to treat depression, SSRIs have moved to the front line of therapeutic options for treating discomforts related to MENOPAUSE such as HOT FLASHES, replacing hormone replacement therapy (HRT).

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)

citalopram	duloxetine
escitalopram	fluoxetine
fluvoxamine	paroxetine
sertraline	

Tetracyclics The tetracyclic class of antidepressants (a four-ringed molecular structure) debuted in the late 1990s as an alternative to the tricyclics. Like tricyclics, the tetracyclics extend the presence of serotonin and norepinephrine by delaying their reuptake. However, tetracyclics have fewer as well as milder side effects than tricyclics.

TETRACYCLIC ANTIDEPRESSANTS

amoxapine	maprotiline
mirtazapine	

Other antidepressants Several new antidepressants came into use in the late 1990s and early 2000s that do not fit within conventional classifications. These drugs selectively affect specific neurotransmitters or neuroreceptors through different mechanisms from those of other antidepressants. Bupropion has US Food and Drug Administration (FDA) approval for use in SMOKING CESSATION efforts.

OTHER ANTIDEPRESSANTS	
bupropion	nefazodone
trazodone	venlafaxine

How These Medications Work

Most antidepressant medications, regardless of class, work through selective reuptake inhibition: they block the natural breakdown and reassimilation of specific neurotransmitters, biochemicals that carry NERVE impulses between neurons. The result is an extended presence of the neurotransmitters, increasing the number of nerve impulses they can transport. Researchers do not know the precise mechanisms of this process, though the result is an elevation of function in the affected parts of the brain, which in the case of depression are areas concerned with mood and emotion. Though antidepressants affect neurotransmission from the first dose, noticeable changes generally do not occur until after several weeks of use.

Therapeutic Applications

The primary use of antidepressant medications is to treat moderate to severe DEPRESSION. Doctors may also prescribe antidepressants to treat BIPOLAR DISORDER, BODY DYSMORPHIC DISORDER, eating disorders, ACUTE STRESS DISORDER, POST-TRAUMATIC STRESS DISORDER (PTSD), POSTPARTUM DEPRESSION; ADDICTION recovery, SEASONAL AFFECTIVE DISORDER (SAD), and in combination with other medications to treat psychotic disorders such as SCHIZOPHRENIA. Some antidepressant medications have uses outside the realm of psychiatric disorders and psychologic conditions, such as smoking cessation, chronic pain management, and relief of menopause discomforts. Some of these are OFF-LABEL USE.

Risks and Side Effects

Though antidepressants make it possible for nearly 10 million Americans to participate fully in, and enjoy, the activities of every day life, they have substantial risks. Any antidepressant that inhibits reuptake of norepinephrine also has an effect on smooth MUSCLE function throughout the body, notably the gastrointestinal tract, genitourinary tract, and cardiovascular system. Side effects such as dry mouth, constipation, urinary hesitancy or urinary frequency, and ERECTILE DYSFUNCTION are common, though they often improve after taking the antidepressant for three months. Though each classification of antidepressant drugs has risks and side effects that are common to all drugs in the classification, each medication also has unique risks and side effects. Often, side effects improve over time and are temporary (go away when the person stops taking the antidepressant).

Excessive serotonin levels can cause serious and potentially life-threatening symptoms, called serotonin syndrome, that affect the functions of the LIVER, HEART, KIDNEYS, and skeletal muscles. It is important not to combine SSRIs with other antidepressants or drugs, including herbal and OVER-THE-COUNTER (OTC) DRUGS, that increase serotonin levels.

Antidepressant medications interact or interfere with numerous other medications including OVER-THE-COUNTER (OTC) DRUGS, herbal, and prescription products. MAOIs interact with numerous foods, decongestant medications, ANTIHISTAMINE MEDICATIONS, and antihypertensive medications (drugs to treat high blood pressure).

See also ANTIANXIETY MEDICATIONS; NEURORECEPTOR; PSYCHOSIS; ST. JOHN'S WORT; SUICIDAL IDEATION AND SUICIDE.

antipsychotic medications Medications to manage the symptoms of psychiatric disorders of PSYCHOSIS, including SCHIZOPHRENIA. The first of these medications, the phenothiazine DRUG chlorpromazine (Thorazine), debuted in the early 1950s and revolutionized treatment for psychotic disorders. Antipsychotic medications, also called neuroleptics, are powerful drugs that affect the ways in which the BRAIN processes information. Conventional antipsychotics are the mainstay of therapy for many psychotic disorders. Novel, or atypical, antipsychotics are newer drugs that attempt to provide a better balance between therapeutic benefit and risk of side effects. They are the first choice treatment for some moderate psychotic disorders.

How These Medications Work

Antipsychotic medications work by altering the balance of neurotransmitters (biochemicals that

conduct electrical impulses among neurons) in the brain. Most antipsychotic medications target DOPAMINE, a NEUROTRANSMITTER that is integral to the functions of thought, reasoning, memory, emotion, and mood. Though researchers do not know what causes psychotic disorders, they believe the ways in which the brain produces and uses dopamine are key factors.

ANTIPSYCHOTIC MEDICATIONS

Conventional	
chlorpromazine	fluphenazine
haloperidol	mesoridazine
perphenazine	pimozide
prochlorperazine	thioridazine
thiothixene	trifluoperazine
trifluopromazine	
Novel (Atypical)	
aripiprazole	clozapine
loxapine	molindone
olanzapine	quetiapine
risperidone	ziprasidone

Therapeutic Applications

Doctors prescribe antipsychotic medications to treat psychotic disorders such as severe BIPOLAR DISORDER, schizophrenia, personality disorders, dissociative disorders, OBSESSIVE–COMPULSIVE DISORDER (OCD), and severe MANIA. Often a therapy regimen includes several medications that address various symptoms. Treatment with antipsychotic medications requires regular and close follow-up to monitor therapeutic effect as well as potential side effects.

Risks and Side Effects

Antipsychotic medications have numerous risks and side effects, many of which are drug specific. The most serious is neuroleptic malignant syndrome (NMS), a constellation of symptoms that may occur at any time during treatment with antipsychotic medications, although it is more likely to develop with sudden high doses. NMS follows a predictable course, starting with MUSCLE rigidity with high FEVER, confusion, and disorientation. Rapid intervention is necessary to stop the antipsychotic medications, reduce the fever, and provide appropriate medical support. Without such intervention, there is high probability that NMS will be fatal.

Dopamine, the primary target of most antipsychotic medications, is also the primary neurotransmitter for NERVE impulses that regulate voluntary movement. Conventional antipsychotics have a broad base of effects in regard to their actions on dopamine receptors. Because of this nonspecific activity, these drugs have high risk for causing neuromuscular complications (drug-induced movement disorders). The most serious of these complications is tardive dyskinesia, a condition of involuntary, rhythmic, repetitious movements. Tardive dyskinesia is a particular risk with phenothiazines and sometimes persists even after stopping the medication. Other possible neuromuscular side effects include tremors and rigidity.

Novel, or atypical, antipsychotic medications target specific dopamine receptors found in greater numbers in the regions of the brain that regulate cognitive and emotional functions. Though novel antipsychotics can cause neuromuscular side effects with prolonged, high-dose use, the side effects are likely to be both less severe and temporary. A rare complication associated with clozapine is severe agranulocytosis, a precipitous drop in the number of white BLOOD cells called granulocytes. Granulocytes are essential for immune function. Because of the potential for this complication, people who take clozapine must have blood tests once a week for the duration of treatment plus four weeks after treatment ends to monitor their white blood cell counts.

Both conventional and novel antipsychotics interact with numerous medications, prescription as well as OVER-THE-COUNTER (OTC) DRUGS and some interact with foods. The longer a person takes antipsychotic medications, the greater the risk for complications or side effects. It is essential that the prescribing psychiatrist regularly and frequently evaluate the effectiveness of treatment and make adjustments as possible to reduce risk. For most people who have serious psychotic disorders, the QUALITY OF LIFE that medications make possible clearly outweighs their potential side effects.

See also ANTIANXIETY MEDICATIONS; ANTIDEPRESSANT MEDICATIONS; DISSOCIATIVE DISORDER; ELECTROCONVULSIVE THERAPY (ECT); GRANULOCYTE; PSYCHOTHERAPY.

attention deficit hyperactivity disorder (ADHD) A behavior disorder, often arising in early childhood, of marked difficulty or inability to concentrate and in particular to sit still. Though in some children symptoms are apparent early in childhood, starting school provides the first insight into ADHD for many children. Key symptoms include

- uncontrolled impulsive behavior
- difficulty listening to others
- poor attention to details
- inability to sit or stand without movement (fidgeting)
- excessive and impulsive talking

The diagnostic path includes comprehensive medical examination and NEUROLOGIC EXAMINATION to rule out physical causes for symptoms. Treatment is often stimulant medications such as methylphenidate, dextroamphetamine, or pemoline, which have the opposite effect of producing calm in children who have ADHD. ANTIDEPRESSANT MEDICATIONS are sometimes more effective for adolescents. Often parents find it beneficial to attend classes or workshops that teach methods for positive reinforcement to encourage more appropriate behaviors. ADHD may persist into adulthood, though many children outgrow most if not all of the symptoms by late ADOLESCENCE.

See also CONDUCT DISORDER; OPPOSITIONAL DEFIANT DISORDER; STIMULANTS.

autism A collective term for a spectrum of developmental disorders, also called autism spectrum disorder or pervasive developmental disorders (PDDs). Symptoms begin in early childhood, typically between the ages of 18 months and 3 years, though when parents look back on the child's infancy they can often detect earlier indications of problems. Autism ranges from mild to incapacitating in severity. Though most children experience abnormal developmental progress from birth, some appear to develop normally and then seem to suddenly disengage from social interaction. Autism is a lifelong condition that, in all but its mildest form, requires ongoing attention and treatment.

Symptoms and Diagnostic Path

The symptoms of autism become more clear as the child passes developmental markers without demonstrating the appropriate level of ability. The first pivotal marker is around age one year, by which time a child should be babbling and freely interacting with other people and his or her environment. The child who has autism, by contrast, often appears socially withdrawn and may stare at a particular toy or object for hours yet not play with it. Other characteristic indications of autism include a child who does not

- smile or make eye contact with other people
- respond to his or her name
- like to be hugged or touched
- attempt to speak or communicate with others
- understand communication efforts from others
- display attachment to or affection toward his or her parents

Many children who have autism engage in repetitious actions that are potentially harmful to themselves, such as banging their heads. The communication difficulties affect both expression and understanding; many children who have autism lack the ability to perceive emotions or to predict how others will respond. They may also fulfill their needs by simply taking what they want, which, until diagnosis, parents and other caregivers may interpret as rudeness or inconsideration. In reality it is neither; it is the only mechanism of communication available to the child at the time.

The diagnostic path includes comprehensive physical examination and NEUROLOGIC EXAMINATION, age-appropriate psychologic evaluations (including those specific for autism), and sometimes GENETIC TESTING (autism is strongly associated with FRAGILE X SYNDROME). Diagnosis is a process of ruling out other conditions and confirming the symptoms of developmental delay.

Treatment Options and Outlook

Treatment is most successful when it begins by age two and consists primarily of extensive therapy to provide simple, clear, and consistent structure for

the child that shapes behavior and mechanisms of communication. This approach ties in with the child's inherent need for repetition and order in his or her personal environment. Older children sometimes benefit from medications such as selective serotonin reuptake inhibitors (SSRIs), ANTIDEPRESSANT MEDICATIONS that appear to help stabilize BRAIN function in autism. Some children whose behavior is aggressive may benefit from ANTIPSYCHOTIC MEDICATIONS, and children who have significant trouble staying focused may benefit from medications used to treat ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Adults who have mild autism (often called higher functioning autism or Asperger's syndrome) are often able to function in work situations, though their lack of social skills may create problems with INTERPERSONAL RELATIONSHIPS. Adults who have moderate autism generally benefit from continuation of a highly structured environment, which may mean continuing to live with parents or other responsible adults. Adults who have severe autism often need the extensive supervision and ongoing care that living in a group home or secure, supervised residential facility provides for them.

Risk Factors and Preventive Measures

The causes of autism are unknown. There has been speculation of a correlation between thimerosal, a mercury-based preservative used in some childhood vaccines, and autism and between autism and environmental exposure to mercury as well as to lead. Researchers continue to study these potential links though so far have found no definitive evidence to clearly support or refute them. There is a known connection between the genetic disorder fragile X syndrome and autism, and researchers suspect though have yet to confirm other genetic causes.

See also GENETIC DISORDERS; HEAVY-METAL POISONING.

B

behavior modification therapy A treatment approach that focuses on changing one's actions to remedy inappropriate responses or behaviors. Behavior modification may be effective for ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD), behavior disorders, PHOBIA, SMOKING CESSATION, WEIGHT LOSS AND WEIGHT MANAGEMENT, and similar issues. The three most common types of behavior modification are

- aversion therapy, which connects the undesired action or behavior with an unpleasant experience
- positive reinforcement therapy, which connects the desired action or behavior with a pleasant experience
- desensitization, which establishes repeated, progressively extensive exposure to a circumstance that produces anxiety to diminish the anxiety response

Behavior modification therapy is most successful in treating narrowly focused conditions. Combining behavior modification therapy with COGNITIVE THERAPY, which helps people recognize thought patterns, greatly improves its success. Therapists sometimes combine behavior modification therapy with HYPNOSIS to increase the person's receptiveness to change.

See also PSYCHOTHERAPY.

bipolar disorder A pattern of alternating MANIA and DEPRESSION (manic episodes and depressive episodes) that often results in significant dysfunction and inability to participate in work and social activities. About two million Americans have bipolar disorder, sometimes called manic–depressive disorder. Though indications of bipolar disorder may be present in ADOLESCENCE, most people do not seek medical attention or receive a diagnosis until they are well into adulthood.

Symptoms and Diagnostic Path

The pattern of symptoms occurring in alternating episodes is as important as the symptoms themselves and helps distinguish bipolar disorder from either depression or mania, though many researchers believe these conditions exist along a

SYMPTOMS OF BIPOLAR DISORDER

Symptoms of Manic Episodes	Symptoms of Depressive Episodes
euphoria and excitability	hopelessness and futility
heightened energy	diminished energy or fatigue
reduced sleep	excessive sleep
spending sprees and other behavioral indiscretions	pessimism about abilities and accomplishments
substance abuse (including ALCOHOL)	chronic physical discomforts and ailments
inability to focus or concentrate	inability to concentrate
rapid, often disjointed speech	difficulty with logic and reasoning
disorganized thoughts	loss of interest in activities, family, and friends
unrealistic perceptions of abilities and accomplishments	thoughts of suicide (suicide ideation)

continuum rather than as discreet disorders. Episodes of symptoms may last from weeks to months. Many people experience periods of normal mood between the episodes of symptoms and may experience extended time periods (sometimes years) without episodes of symptoms.

Some people experience a mix of depressive and manic symptoms with each episode, which often causes significant agitation and inability to function. Severe episodes of either depression or mania may include symptoms of psychosis (detachment from reality) such as DELUSION, HALLUCINATION, and bizarre behavior.

The diagnostic path includes comprehensive physical examination and NEUROLOGIC EXAMINATION, psychologic evaluation, and often testing for ALCOHOL or substance abuse. The doctor may also evaluate THYROID GLAND function because some people in whom manic episodes dominate have chronic HYPOTHYROIDISM (low thyroid gland function). In general, diagnostic criteria include the existence of five or more symptoms during each episode of symptoms that extend for two weeks or longer. Shorter cycles or briefer episodes may indicate similar though less severe disorders such as CYCLOTHYMIC DISORDER. Psychiatrists further classify bipolar disorder according to the pattern of symptoms:

- Bipolar I disorder is classic bipolar disorder, with depressive and manic symptoms of equal severity and length of episode.
- Bipolar II disorder features mild, short manic episodes though full depressive episodes.
- Rapid-cycling bipolar disorder features short though full-symptom cycles of episodes that occur four times a year or more frequently.

Doctors commonly consider responsiveness to treatment as affirmation of the diagnosis.

Treatment Options and Outlook

Nearly everyone who has bipolar disorder requires long-term treatment with medication to moderate symptoms. These medications include

- lithium carbonate or lithium citrate, a mood stabilizing DRUG especially effective for controlling manic symptoms
- antiseizure medications such as valproic acid (valproate), carbamazepine, gabapentin, and topiramate
- novel (atypical) ANTIPSYCHOTIC MEDICATIONS such as clozapine, olanzapine, risperidone, quetiapine, and ziprasidone, which have mood stabilizing effects
- ELECTROCONVULSIVE THERAPY (ECT) when medications are not effective or symptoms are severe
- forms of psychotherapy that help the person develop behaviors and methods for managing symptoms when they do occur
- methods to reduce stress

People who have hypothyroidism also require thyroid HORMONE supplementation; long-term treatment with lithium can cause hypothyroidism as well. Bipolar disorder is a lifelong condition that requires ongoing, consistent treatment.

Risk Factors and Preventive Measures

Family history is the most significant risk factor for bipolar disorder. However, researchers do not know what causes bipolar disorder, and there are no measures to prevent it from developing. Early diagnosis and consistent treatment are most effective for reducing the severity and disruptiveness of symptoms and often can prevent the condition from worsening.

See also STRESS AND STRESS MANAGEMENT.

body dysmorphic disorder A condition of DELUSION in which the person focuses obsessively on a slight flaw or perceived imperfection of a particular body part to the extent of persistently seeking medical care to "fix" the problem. The focus is so intense that it interferes with the person's social and educational or professional interactions. The person may stand in front of a mirror for hours staring at the body part, engage in ritualistic behavior such as manipulating the part into the desired appearance, or refuse to go out in public without covering the part to somehow mask it. Some people avoid mirrors and reflective surfaces to the extent of refusing to go to stores or office buildings that have glass doors.

A person consumed with concern about his or her ears, for example, might spend several hours

every morning holding the ears flat against the head then letting go to see whether they've changed, repeating this behavior to the extent of missing school or work. The person may go out in public only if wearing a hat regardless of whether a hat is appropriate and may refuse to get haircuts for fear that the hair stylist will see his or her ears. The person may have multiple cosmetic surgery operations to obtain a more satisfactory appearance but is never happy with the results.

Because body image is highly subjective and most people do have minor imperfections or asymmetries in appearance, a first or even second cosmetic surgery procedure may not seem out of the ordinary. It is when the person persists in attempts to "fix" the "problem" that the dysfunction becomes apparent. The plastic surgeon or dermatologist the person consults for cosmetic surgery may be the first to raise a red flag about the person's obsession. The most successful treatment approach is medication therapy with a selective serotonin reuptake inhibitor (SSRI), a class of ANTIDEPRESSANT MEDICATIONS. Most people experience marked improvement within three months and have long-term improvement after six months to a year of medication. Combining SSRI therapy with COGNITIVE THERAPY has more rapid effectiveness for many people, though cognitive therapy alone is far less effective than SSRI therapy alone. Most people are able to reach a level of normal perspective about body image and return to full function within daily life.

See also DEPRESSION; EATING DISORDERS; GENERAL ANXIETY DISORDER (GAD); OBSESSIVE–COMPULSIVE DISORDER; PLASTIC SURGERY; SOMATIZATION DISORDER.

brief reactive psychosis A trauma- or stress-induced psychotic episode (break with reality) that lasts longer than one day but less than one month. Symptoms may include HALLUCINATION, DELUSION, disordered speech, nonsensical expressions or thought processes, and strange or bizarre behavior such as outbursts of laughing without provocation or sitting motionless for hours and then returning to normal activities as though nothing out of the ordinary had happened. Often the episode is more apparent to others than to the person and may end before there is enough concern for family, friends, or co-workers to seek medical attention for the person. When symptoms result in a doctor's evaluation, treatment may be a combination of short-term ANTIPSYCHOTIC MEDICATIONS and PSYCHOTHERAPY to address the underlying trauma or stress. Treatment usually resolves the psychotic episode.

See also ACUTE STRESS DISORDER; COGNITIVE FUNCTION AND DYSFUNCTION; STRESS AND STRESS MANAGEMENT.

C

cognitive therapy A therapy approach that helps a person recognize negative or unhelpful thought patterns and replace them with positive and helpful ones. Though there are different forms of cognitive therapy, the underlying foundation of cognitive therapy establishes thought as the basis for emotion and behavior. Conscious awareness of one's thoughts thus provides the ability to change one's emotions (feelings) and behaviors (actions).

Cognitive therapy is often effective treatment for DEPRESSION, GENERAL ANXIETY DISORDER (GAD), BIPOLAR DISORDER, and similar psychologic conditions. Cognitive therapy tends to produce results more rapidly (less than 20 visits with the therapist) than many other methods of therapy. This brevity is especially appealing to people who do not have the resources or time to undergo conventional PSYCHOTHERAPY, which often takes years before progress is apparent.

See also BEHAVIOR MODIFICATION THERAPY; MIND–BODY INTERACTIONS.

conduct disorder A behavioral disorder in which a child engages in behaviors that disregard social norms and the rights of others. A child who has conduct disorder may frequently become involved in fights, be truant from school, be in trouble at school, bully others, shoplift, or run away from home. The diagnostic path includes a comprehensive medical examination to rule out physical causes for symptoms and may include evaluation for substance abuse. Treatment is often a combination of BEHAVIOR MODIFICATION THERAPY and COGNITIVE THERAPY for the child individually and sometimes also for the family. Appropriate intervention and treatment can turn the cycle of destructive behavior before it results in long-term consequences.

See also ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD); OPPOSITIONAL DEFIANT DISORDER.

conversion disorder The expression of emotional issues through physical symptoms that typically come on suddenly, often after a traumatic experience, and commonly involve some sort of debilitating loss of function such as inability to see or apparent PARALYSIS of an extremity. Older terminology for such losses includes hysterical blindness and hysterical paralysis.

The concern the person feels and expresses about the loss is disproportionately minor, and the doctor is unable to detect any physiologic or physical causes for the symptoms. Most often the episode of symptoms resolves on its own within a few weeks, as the precipitating emotional or psychologic concern improves or goes away. PSYCHOTHERAPY, COGNITIVE THERAPY, or BEHAVIOR MODIFICATION THERAPY is often effective treatment. It is also important to provide appropriate care for the involved function, such as passive exercise for apparently paralyzed limbs to prevent the muscles from atrophying.

See also ACUTE STRESS DISORDER; BODY DYSMORPHIC DISORDER; BRIEF REACTIVE PSYCHOSIS; COPING MECHANISMS; EATING DISORDERS; FACTITIOUS DISORDERS; HYPOCHONDRIASIS; MIND–BODY INTERACTIONS; SOMATIZATION DISORDER; STRESS AND STRESS MANAGEMENT.

coping mechanisms The emotional and behavioral strategies people use to accommodate and recover from stressful circumstances in their lives over which they have little control. Numerous extrinsic and intrinsic factors shape and influence the coping mechanisms available to an individual. Among these factors are

- culture and generation
- financial or economic status
- personal experiences with crisis or disaster
- seriousness of the situation

Coping mechanisms, when they are positive, move a person toward regaining control over the situation and the ability to manage its circumstances. When they are negative, coping mechanisms often instead result in responses that perpetuate dysfunction or even the crisis itself. Because coping mechanisms are learned behaviors, it is possible for people to identify those that do not work well for them and replace them with others that are more successful.

See also ANGER AND ANGER MANAGEMENT; BEHAVIOR MODIFICATION THERAPY; COGNITIVE THERAPY; PSYCHOTHERAPY; STRESS AND STRESS MANAGEMENT.

cyclothymic disorder Alternating, short-term periods (usually days) of elation and melancholy, milder than the cyclic periods of MANIA and DEPRESSION that define BIPOLAR DISORDER. Other people commonly view the person as extremely moody or emotionally fragile though able to function reasonably well in work and social settings when at either mood extreme and quite well during periods of mood moderation. Some psychiatrists consider cyclothymic disorder, also called cyclothymia, to be a precursor (precondition) to bipolar disorder though other psychiatrists consider it a separate condition.

COGNITIVE THERAPY and BEHAVIOR MODIFICATION THERAPY are the most effective treatments, providing understanding of the disorder and teaching ways to accommodate the extremes of the mood swings so as to maintain appropriate interactions with others. Medications used to treat bipolar disorder may improve symptoms that disrupt the person's ability to function (such as job performance or fulfilling family responsibilities). Alternative and complementary approaches such as BIOFEEDBACK and HYPNOSIS may also improve the person's ability to cope with mood extremes.

See also COPING MECHANISMS.

D

delusion A false perception or belief that persists even in confrontation with a reality that demonstrates its falseness. There may be an element of absurdity or bizarreness to the delusion or the delusion may appear to have some plausibility until closer examination refutes it. Many people have delusions yet function normally in the world. Delusions of persecution, being followed or watched, or infidelity in a relationship can result in behaviors that cause distress for the person and for others. There is no particular treatment for delusions. Delusions are also common components of psychotic disorders such as SCHIZOPHRENIA, in which case treatment attempts to manage symptoms of the disorder overall.

See also COGNITIVE FUNCTION AND DYSFUNCTION; HALLUCINATION; PARANOIA; PSYCHOSIS.

depression A psychologic condition of diminished emotional, cognitive, and physical function. Everyone feels sad and out of sorts with the events in their lives at some point. When these feelings interfere with the activities of daily life, they constitute clinical depression (also called major depression), a health condition that requires medical treatment. About 25 percent of adults and 12 percent of teens in the United States have depression, though fewer than half seek treatment.

Suicide is a significant risk in untreated depression. It is important to take seriously statements people make about taking their own lives or "ending it" and to do what is possible to help them get appropriate evaluation and care.

Symptoms and Diagnostic Path

The common symptoms of depression include

- feeling hopeless, worthless, helpless, or empty
- loss of interest in activities, work, friends, and family
- diminished LIBIDO (interest in sex), SEXUAL DYSFUNCTION, or ERECTILE DYSFUNCTION
- difficulty concentrating and remembering
- sleep disturbances—sleeping all the time, being unable to sleep, or changes in the usual sleep pattern
- chronic HEADACHE, gastrointestinal distress, or body aches and discomforts that do not have apparent cause or respond to efforts to relieve them
- irritability, short temper, restlessness
- thoughts of death or ways to take one's own life

The diagnostic path begins with a comprehensive physical examination, NEUROLOGIC EXAMINATION, and evaluation for substance abuse because numerous common health conditions (such as untreated HYPOTHYROIDISM or ANEMIA) and many drugs can cause symptoms of depression. Further evaluation includes psychologic assessment and an attempt to determine whether the person may be contemplating suicide.

Treatment Options and Outlook

About 80 percent of people who have depression take ANTIDEPRESSANT MEDICATIONS, some as sole treatment and others in combination with PSYCHOTHERAPY. The most commonly prescribed anti-

depressants are the selective serotonin reuptake inhibitors (SSRIs), which became available in the 1990s. Psychotherapy alone is sufficient treatment for some people who have mild symptoms. There are numerous types of psychotherapy, some of which are able to make rapid progress in improving symptoms and others that extend over months to years in an effort to fully expose, understand, and address the issues underlying the depression.

Alternative and complementary therapies that are often helpful include ACUPUNCTURE, MEDITATION and other stress relief measures, and mind–body approaches such as YOGA and TAI CHI. A number of studies show that one to two hours of physical exercise daily has the same effect as commonly prescribed antidepressant medications on reducing symptoms of mild to moderate depression. The herbal remedy ST. JOHN'S WORT, available without a doctor's prescription as a dietary supplement in the United States, also may relieve symptoms of depression as effectively as prescription antidepressant medications. Many European countries regulate St. John's wort as a prescription product and doctors prescribe it as a first-line treatment for mild to moderate depression.

Do not take ST. JOHN'S WORT when taking a prescription antidepressant. Doing so can result in a potentially life-threatening complication called serotonin syndrome.

ELECTROCONVULSIVE THERAPY (ECT), which uses electricity to momentarily disrupt the NERVE signals in the BRAIN, is an effective treatment for severe depression that does not improve with medications or for people who cannot take antidepressants.

Risk Factors and Preventive Measures

Family history is a significant factor for developing depression or related conditions such as CYCLOTHYMIC DISORDER, BIPOLAR DISORDER, and DYSTHYMIC DISORDER. Depression may also develop in reaction to persistent, intense stress or a traumatic event such as the death of a loved one or diagnosis with a serious physical illness such as CARDIOVASCULAR DISEASE (CVD) or cancer.

Hormonal shifts in menstruating women increase the risk for depression; women who have substantial PREMENSTRUAL SYNDROME (PMS) symptoms also have a higher likelihood for developing depression. As well, nearly all women experience mild depressive symptoms in the first few weeks after childbirth and up to 20 percent develop full depression (POSTPARTUM DEPRESSION) that may last as long as a year.

Researchers also have identified proteins associated with depression that either are missing or are present in high levels. Early diagnosis and initiation of treatment are the most effective measures for heading off serious depression, though there are no measures to actually prevent depression from developing.

See also EXERCISE AND HEALTH RISK REDUCTION; GENERALIZED ANXIETY DISORDER (GAD); HORMONE; MENSTRUAL CYCLE; POST-TRAUMATIC STRESS DISORDER (PTSD); SUICIDAL IDEATION AND SUICIDE.

dissociative disorder A psychiatric disorder in which a person creates intentional though often not conscious separation between self and a traumatic event. The most common form of dissociative disorder is dissociative amnesia, a form of memory loss in which the person does not remember the circumstances of a trauma, such as childhood abuse or SEXUAL ASSAULT, and may not remember that the events occurred at all. Amnesia episodes are generally brief and contained to specific periods of time.

In dissociative fugue the amnesia is more extensive and the person may adopt a new identity and life, believing he or she is the created identity and dissociating entirely from the real identity and life. Dissociative fugue typically follows a significant trauma, such as living through a major natural disaster. The person may assume the created identity for months and sometimes years. Though dissociative fugue often appears as an attempt to walk away from difficulties or responsibilities, the person may not remember the fugue upon returning to his or her real identity.

The most extreme form of dissociative disorder is dissociative identity disorder (previously called multiple personality disorder) in which one person has two or more personalities. A person who has dissociative identity disorder typically experienced overwhelming trauma, such as abuse or the loss of a parent or other family members, in child-

hood at a time of vulnerability in personal development of sense of self. The various personalities may know of each other or be unaware that the others exist. Dissociative identity disorder is highly debilitating.

Treatment may combine ANTIPSYCHOTIC MEDICATIONS and intensive PSYCHOTHERAPY. The extent to which treatment succeeds depends on multiple factors, which are difficult to predict at the onset of treatment. RECURRENCE and relapse are common.

See also ACUTE STRESS DISORDER; BRIEF REACTIVE PSYCHOSIS.

dysthymic disorder Low-intensity, long-term or chronic DEPRESSION. A key characteristic of dysthymic disorder, also called dysthymia, is that the person is generally able to function in the world though does not feel much joy or pleasure. Irritability, tiredness, and disinterest in most activities are other hallmark symptoms. Treatment that combines therapy (such as COGNITIVE THERAPY or BEHAVIORAL MODIFICATION THERAPY) and ANTIDEPRESSANT MEDICATIONS is often effective in diminishing symptoms and helping affected people learn productive COPING MECHANISMS to accommodate aspects of their lives that cause stress. Alternative and complementary methods such as BIOFEEDBACK, HYPNOSIS, MEDITATION, and VISUALIZATION are often helpful for reducing symptoms as well as restoring a sense of control about the person's life circumstances.

See also ST. JOHN'S WORT; STRESS AND STRESS MANAGEMENT.

E–I

eating disorders Psychologic conditions in which the person restricts food intake because of the belief that he or she is overweight. Eating disorders affect 10 times as many girls and women as boys and men. There are two main types of eating disorder: anorexia nervosa and bulimia nervosa.

Anorexia nervosa With anorexia nervosa, the person avoids eating, eats only very small amounts of certain foods, vomits after eating, or excessively uses laxatives and diuretics to reduce body weight. Some people who have anorexia nervosa also exercise compulsively and excessively to further drive down body weight. The person weighs herself numerous times each day, often following obsessive rituals (such as spitting or urinating before stepping on the scale, completely undressing, or taking off jewelry) to obtain the lowest weight possible. Even when weight reaches an unhealthy low, the person still believes she is overweight.

Bulimia nervosa In bulimia the person compulsively binges (eats excessive amounts of food in a short period of time), then compensates through inappropriate behaviors, such as induced vomiting or excessive laxative use, to eliminate the food. People who have bulimia often remain at normal weight or slightly below because they do consume calories during binging episodes, though believe they are excessively overweight.

Symptoms and Diagnostic Path

Because eating disorders incorporate secretive behaviors, symptoms may be subtle until weight loss (in anorexia particularly) is severe. Indications of an eating disorder include

- moving food around on the plate but not eating any of it
- self-proclaimed weight "problems" though excessively thin
- delayed or irregular MENSTRUATION
- going to the bathroom during or immediately after meals
- supplies of laxatives, diuretics, and enemas
- damaged tooth enamel (from vomiting)

The diagnostic path includes a comprehensive physical examination to detect signs of malnourishment or damage to the body resulting from prolonged inadequate nutrition. The KIDNEYS and HEART are most vulnerable to such damage.

Treatment Options and Outlook

The standard of care for treatment is a three-level approach:

- restoring body weight to a healthy range, which may require nutritional support or supplementation as well as supervised meals
- PSYCHOTHERAPY
- ANTIDEPRESSANT MEDICATIONS, usually selective serotonin reuptake inhibitors (SSRIs)

Treatment for anorexia is often a long-term process; treatment for bulimia tends to be more effective. Some people recover fully, though many deal with eating issues for most of their lives. SUDDEN CARDIAC DEATH remains a lifelong risk in people who have anorexia.

Risk Factors and Preventive Measures

Researchers do not know what causes eating disorders though believe they result from an interplay of genetic and environmental or psychosocial factors such as family relationships and self-

esteem issues. Though eating disorders are not preventable, early intervention and treatment can prevent further health conditions and minimize the damage to the body that severe food deprivation causes.

See also BODY DYSMORPHIC DISORDER; DEPRESSION; DIET AND HEALTH; NUTRITIONAL NEEDS; OBESITY; SOMATIZATION DISORDER; STARVATION.

electroconvulsive therapy (ECT) A treatment for severe DEPRESSION that does not respond to treatment with ANTIDEPRESSANT MEDICATIONS. ECT is also sometimes effective for severe MANIA or BIPOLAR DISORDER when either condition fails to improve with other treatments. ECT uses a mild electric shock to the outside of the skull to momentarily disrupt the electrical activity of the BRAIN. The disruption causes the brain to release a flood of neurotransmitters, such as serotonin, DOPAMINE, EPINEPHRINE, and NOREPINEPHRINE. These neurotransmitters, which are biochemical messengers that convey electrical impulses among the neurons (NERVE cells) in the brain, strongly affect mood and emotion. The typical course of treatment with ECT is up to 3 treatments per week for as many as four weeks (12 treatments total).

The psychiatrist performs ECT after the person receives general ANESTHESIA, applying electrodes one on each side of the person's head. The actual discharge of electrical energy lasts about two seconds. Medications to relax the muscles and block their ability to receive messages from the brain during the treatment prevent the body from reacting to the seizures occurring in the brain. The person emerges from the anesthesia about 10 minutes after the shock and goes to the recovery room until fully awake. Some people experience short-term memory loss and brief cognitive dysfunction or disorganization of thoughts for a short time after the ECT.

See also COGNITIVE FUNCTION AND DYSFUNCTION; MEMORY AND MEMORY IMPAIRMENT; NEURON; NEUROTRANSMITTER.

factitious disorders Psychiatric conditions in which the person contrives the symptoms of an illness (physical or psychologic). Despite the purposeful contrivance of symptoms, the person is unable to stop the behavior. The factitious disorder may have symptoms that are primarily psychologic, primarily physical (also called Munchausen syndrome), or a combination of psychologic and physical. People who have factitious disorders often see multiple doctors in different clinics and hospitals and sometimes in different cities. Frequently they have undergone numerous invasive procedures and surgeries by the time doctors begin to realize a psychiatric condition is underlying. Characteristics of factitious disorders include

- persistent symptoms that are inconsistent with diagnostic findings
- symptoms that change after treatment begins
- eagerness to undergo invasive procedures and surgeries
- unwillingness to allow current health-care providers to consult with previous health-care providers
- reliable treatments fail to work in the expected ways

Diagnosis of factitious disorders is difficult because the person typically denies any element of contrivance about his or her health problems and symptoms despite confrontation with evidence such as test results. The concern is twofold: The person may do serious harm to himself or herself through the creation of symptoms or treatment for them, and the person extensively consumes expensive and often limited medical resources. Another person, such as a family member, who knows of the factitious disorder can sometimes mitigate the risks to the person's well-being by alerting health-care providers. However, overall, treatment for factitious disorders (and especially Munchausen's syndrome) is not very successful.

Factitious disorder by proxy, also called Munchausen's syndrome by proxy, is a variant in which the person creates symptoms in another person, often under the guise of caring for the person, and then steps into the role of seeking medical attention for the person. Munchausen's syndrome by proxy most commonly involves a parent (usually mother) who creates symptoms in a child; less common manifestations include an adult child who creates symptoms in a parent or a

spouse who creates symptoms in the other spouse. In Munchausen's syndrome by proxy, which may have legal consequences, protection of the other person is of utmost importance.

See also CHILD ABUSE; DOMESTIC VIOLENCE; ELDER ABUSE; SOMATIZATION DISORDERS.

generalized anxiety disorder (GAD) A psychologic condition in which the person experiences exaggerated worry and anxiety that generates physical symptoms such as excessive sweating, trembling, and tics or MUSCLE twitches. Gastrointestinal symptoms, such as NAUSEA and DIARRHEA, are also common. Symptoms may be episodic (come and go) or persistent (always present) and often interfere with, though do not prevent, the person's function in the world. People who have GAD commonly have other psychologic conditions as well, such as DEPRESSION, OBSESSIVE–COMPULSIVE DISORDER (OCD), POST-TRAUMATIC STRESS DISORDER (PTSD), PANIC DISORDER, or PHOBIA.

After medical and NEUROLOGIC EXAMINATION to rule out organic or neurologic causes for symptoms, the doctor is likely to recommend treatment that combines PSYCHOTHERAPY and ANTIANXIETY MEDICATIONS. Some people also benefit from ANTIDEPRESSANT MEDICATIONS (notably selective serotonin reuptake inhibitors; SSRIs), which further reduce agitation and provide a more balanced emotional landscape. For some people GAD is a limited condition that, once successfully treated, does not return. For many people, however, GAD is a chronic or recurrent condition that periodically requires treatment. Researchers do not know what causes GAD, and there are no measures to prevent its development.

See also ORGANIC BRAIN SYNDROME; PARKINSON'S DISEASE.

hallucination A false sensory perception such as hearing voices or seeing objects that are not there. Hallucinations may affect any or a combination of the five senses—vision, hearing, taste, touch, and smell. Hallucinations may occur in numerous psychiatric conditions as well as neurologic conditions such as ALZHEIMER'S DISEASE and PARKINSON'S DISEASE. They may also occur as undesired side effects of numerous medications and sometimes with high FEVER. A hallucination is entirely real to the person experiencing it. When the cause of persistent hallucination is not clear, the doctor may undertake comprehensive NEUROLOGIC EXAMINATION and psychiatric examination.

See also COGNITIVE FUNCTION AND DYSFUNCTION; DELUSION.

hypochondriasis Obsessive fear that something is wrong with one's physical health. Though it is normal to worry about health, even inappropriately or excessively at times, the person who has hypochondriasis is inordinately preoccupied with observations of natural body functions that he or she perceives as indications of illness. This worry may be so overwhelming as to periodically prevent the person from engaging in normal activities. The person frequently sees health-care providers to evaluate these perceived symptoms. COGNITIVE THERAPY and BEHAVIOR MODIFICATION THERAPY are often successful in helping people recognize and understand the dysfunctional nature of their health worries and learn ways to manage their worry and anxiety. HYPNOSIS is also sometimes helpful.

See also BODY DYSMORPHIC DISORDER; CONVERSION DISORDER; FACTITIOUS DISORDERS; SOMATIZATION DISORDER; STRESS AND STRESS MANAGEMENT.

insanity A legal term within the practice of medicine that identifies the circumstance in which a person is cognitively or emotionally unable to make decisions and manage his or her affairs, including matters related to health care. In matters of law, a clinical diagnosis of insanity generally means a person was unaware of the difference between right and wrong at the time of a specific action, though in the United States this varies among states. Insanity is not a clinical diagnosis.

See also NERVOUS BREAKDOWN.

M–O

mania A psychotic disorder of extremely elevated mood. A person who has mania, also called manic disorder, may appear euphoric and energetic almost to a level of hyperactivity though also is characteristically irritable and impatient. The person often cannot sleep and expresses jumbled, sometimes irrational thoughts and ideas. Mania distorts a person's judgment and can result in inappropriate behaviors such as uncontrolled spending or sexual indiscretions. The diagnostic path includes comprehensive medical examination including BLOOD tests to check for conditions such as HYPERTHYROIDISM (overactive THYROID GLAND) or other endocrine disturbances that could account for symptoms. Medications to treat mania include

- the antiseizure medications valproic acid (valproate), gabapentin, carbamazepine, and topiramate
- the ANTIPSYCHOTIC MEDICATIONS olanzapine, ziprasidone, quetiapine, clozapine, and risperidone
- the mood stabilizer lithium

With treatment the symptoms of mania are manageable and most people are able to return to functional, productive lifestyles. Failure to continue taking medications, a common concern, can result in a return of symptoms.

See also BIPOLAR DISORDER; DEPRESSION; PSYCHOSIS.

multiple personality disorder See DISSOCIATIVE DISORDER.

Munchausen syndrome See FACTITIOUS DISORDERS.

nervous breakdown A casual term for an acute psychiatric condition that suddenly manifests symptoms in a person who had otherwise appeared normal and functional. The underlying premise of a nervous breakdown is that the person reaches his or her breaking point as a consequence of accumulated mental stress or of a single, traumatic precipitating event, such as the death of a loved one. The term *nervous breakdown* came into vogue in the early decades of the 20th century as an attempt to attribute physical causes to mental illnesses. Common usage broadly applied the term to numerous conditions though typically referred to those from which the person eventually recovered.

See also ACUTE STRESS DISORDER; BIPOLAR DISORDER; BRIEF REACTIVE PSYCHOSIS; DEPRESSION; GENERALIZED ANXIETY DISORDER (GAD); POST-TRAUMATIC STRESS DISORDER; SCHIZOPHRENIA.

neurosis A pattern of thought or behavior that causes disruption in a person's life but does not prevent the person from functioning in daily activities and does not represent a break from reality. Nearly everyone has some neuroses, which commonly arise from ineffective COPING MECHANISMS. Neurotic behaviors may include minor compulsive acts (such as starting a set of stairs with the same foot first or sitting in a particular row of seats at the movie theater), excessive worrying, or irrationally avoiding certain circumstances (such as elevators because of fear of getting stuck). Most mental health professionals do not consider neurosis a mental illness.

See also OBSESSIVE–COMPULSIVE DISORDER (OCD); PHOBIA; PSYCHOSIS.

obsessive–compulsive disorder (OCD) A psychiatric disorder in which the person engages in ritualistic, often repetitive behaviors to an extent that interferes with, and may prevent, normal function in everyday activities. OCD is a type of anxiety disorder in which unreasonable worry crafts the ritualistic behaviors, which are dysfunctional methods for accommodating the worry. For example, washing the hands seven times each after going to the bathroom may be an accommodation for an unrealistic worry about, or fear of, infectious disease. Walking three times up and down the sidewalk before entering the house when returning from work may be an accommodation for the unfounded fear of an intruder being in the house or to affirm the presence of someone who is supposed to be there.

The person generally has no conscious desire to engage in the behaviors and may instead consciously desire not to engage in them but is unable to stop. This desire may become so intense as to cause the person to avoid circumstances that activate the behavior—for example, not using public bathrooms to avoid hand washing rituals or entering the home from the garage or back door to avoid entry rituals. OCD begins in childhood for many people and often progresses in adulthood. Other psychologic conditions, such as DEPRESSION and PANIC DISORDER, are also common in people who have OCD.

ANTIANXIETY MEDICATIONS and ANTIDEPRESSANT MEDICATIONS, notably selective serotonin reuptake inhibitors (SSRIs) and tricyclics, are often effective in relieving symptoms. The tricyclic antidepressants clomipramine and imipramine are especially effective. BEHAVIORAL MODIFICATION THERAPY and COGNITIVE THERAPY help the person gain control over his or her thoughts and actions regarding compulsive behaviors. OCD, like other psychologic conditions, likely has genetic as well as environmental foundations. For many people OCD is a chronic condition that requires lifelong treatment, though treatment successfully manages symptoms to allow normal participation in daily life, work situations, and social interactions.

See also GENERALIZED ANXIETY DISORDER (GAD); NEUROSIS; PSYCHOSIS.

oppositional defiant disorder A behavior disorder in which a child expresses open defiance and constant challenge toward parents, teachers, and other adult authority figures. The behaviors appear intended to create irritation and annoyance and consist of

- persistent arguing with adults
- questioning or refusing to follow rules
- deliberately hurtful comments
- perpetually angry demeanor

The expression of defiant behaviors commonly occurs during two periods: around age three and at ADOLESCENCE. Some researchers believe oppositional defiant disorder reflects difficulty the child experiences in the attempt to separate from parents or primary caregivers to establish his or her independent identity.

The diagnostic path begins with a comprehensive medical examination to rule out physical causes for symptoms and may include evaluation for substance abuse. Treatment is often a combination of BEHAVIOR MODIFICATION THERAPY and COGNITIVE THERAPY for the child individually and sometimes for the whole family. Most children respond to treatment.

See also ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD); CONDUCT DISORDER.

P

panic disorder A psychologic condition in which a person feels extreme fear or panic without provocation (unlike PHOBIA, which triggers fear only when facing confrontation with the focus of the phobia). Such panic attacks are the hallmark symptoms of panic disorder and often occur without warning. Symptoms of panic attack can be severe enough to mimic HEART ATTACK and include

- racing HEART RATE (pulse) and rapid BREATHING or difficulty breathing
- profuse sweating or cold sweat
- CHEST PAIN
- HEADACHE
- tingling in the toes and fingers

The diagnostic path begins with a prompt assessment to rule out cardiovascular causes (such as MITRAL VALVE PROLAPSE, heart attack, or STROKE) for the symptoms. The most effective treatment for panic disorder is a combination of BEHAVIOR MODIFICATION THERAPY and COGNITIVE THERAPY. Relaxation and stress management techniques, HYPNOSIS, and sometimes BIOFEEDBACK can help the person cope with panic attacks when they occur. Some people further benefit from short-term treatment with ANTIANXIETY MEDICATIONS. With treatment many people are able to overcome panic disorder.

See also ACUTE STRESS DISORDER; GENERALIZED ANXIETY DISORDER (GAD); STRESS AND STRESS MANAGEMENT.

paranoia A person's unfounded and often disabling suspicion or fear that others are watching, following, or in some other fashion persecuting the person. Paranoia is most commonly a component of psychotic disorders such as SCHIZOPHRENIA though may occur in milder form as a DELUSION (sometimes called delusional disorder when it persists). Often it is a family member who brings the person for treatment because the person's expressions or behaviors turn violent.

Paranoia is difficult to treat because the person's suspicion prevents him or her from seeking care or trusting doctors. ANTIPSYCHOTIC MEDICATIONS and PSYCHOTHERAPY may reduce the intensity of the paranoia, particularly when other psychiatric issues are under control. Paranoia may also be a symptom of degenerative neurologic disorders such as ALZHEIMER'S DISEASE, ORGANIC BRAIN SYNDROME, and BRAIN damage due to TRAUMATIC BRAIN INJURY (TBI) or STROKE.

See also COGNITIVE FUNCTION AND DYSFUNCTION; HALLUCINATION; PSYCHOSIS; VIOLENCE.

pervasive developmental disorders (PDD) See AUTISM.

phobia An intense, irrational fear that prevents the person from normal function and interaction. A phobia such as agoraphobia (fear of public places) or social phobia (fear of being in groups of people) may keep the person from participating in activities vital to the ability to function in the world. Other phobias are specific and are easier to avoid, such as arachnophobia (fear of spiders) or pyrophobia (fear of fire). BEHAVIOR MODIFICATION THERAPY, which teaches behavior methods for overcoming the phobia, and COGNITIVE THERAPY, which teaches understanding of the thinking patterns that result in phobias, often succeed in managing long-term phobic symptoms. Gradual, controlled exposures to the circumstance that causes the fear effectively cures the phobia for many people.

COMMON PHOBIAS

acrophobia	fear of heights
agoraphobia	fear of open spaces or crowded public places
altophobia	fear of heights
aviophobia	fear of flying
claustrophobia	fear of enclosed spaces
herpetophobia	fear of snakes
hydrophobia	fear of water
pyrophobia	fear of fire
sociophobia	fear of being in social gatherings and events
technophobia	fear of technology
xenophobia	fear of strangers

See also OBSESSIVE–COMPULSIVE DISORDER (OCD).

postpartum depression A depressive disorder that occurs after CHILDBIRTH. Postpartum depression may affect as many as 20 percent of women who have recently given birth. Although postpartum depression is more likely to occur in subsequent pregnancies if the woman experienced it after one PREGNANCY, it can develop in women who had previous pregnancies without postpartum depression. It is common for women to feel somewhat sad after giving birth, but these feelings generally pass within a few weeks, and doctors believe they result from the hormonal shifts taking place in the woman's body.

Postpartum depression occurs when the feelings deepen into sensations of hopelessness, being overwhelmed, extreme mood swings, or being inadequate as a mother. Postpartum depression, like other depressive disorders, is a serious clinical condition that requires medical evaluation and treatment. The most effective treatment is PSYCHOTHERAPY in combination with ANTIDEPRESSANT MEDICATIONS. Most women recover with six months to a year, though in some women the depressive disorder becomes chronic and requires ongoing treatment.

A rare complication of postpartum depression is postpartum PSYCHOSIS, in which the woman experiences a complete break with reality and requires intense care, usually in an inpatient setting. Doctors treat postpartum psychosis as any other psychosis, with ANTIPSYCHOTIC MEDICATIONS and psychotherapy. Postpartum psychosis is very severe and likely to return if the woman has another pregnancy.

See also PARENTING; POST-TRAUMATIC STRESS DISORDER (PTSD); STRESS AND STRESS MANAGEMENT.

post-traumatic stress disorder (PTSD) A delayed-onset anxiety disorder that develops months to years after a traumatic experience or event. The event may be personal, such as SEXUAL ASSAULT or CHILD ABUSE, or a widespread disaster such as surviving a plane crash or tornado. Though the first awareness of PTSD symptoms came from soldiers returning from war with "battle fatigue," PTSD can affect anyone who has had a traumatic experience; more than five million Americans have PTSD.

Symptoms and Diagnostic Path

Ordinary events and experiences not obviously related to the trauma may trigger symptoms, and symptoms often worsen at the anniversary of the experience or event. Common symptoms of PTSD include

- flashbacks and nightmares of the traumatic event
- a sense of emotional numbness or distance
- panic-like reactions to places, people, and circumstances that evoke memories of the trauma
- feelings of guilt or unworthiness about surviving when others died

The diagnostic path includes a medical examination to rule out physical causes for symptoms as well as comprehensive psychologic evaluation to distinguish PTSD from other psychologic disorders.

Treatment Options and Outlook

The most effective treatment approach is a combination of PSYCHOTHERAPY and ANTIANXIETY MEDICATIONS or ANTIDEPRESSANT MEDICATIONS. The process of uncovering the event or experience is sometimes extensive, particularly in the case of childhood abuse or trauma. Sometimes the person has a diagnosis of GENERAL ANXIETY DISORDER (GAD) or DEPRESSION then discovers through therapy the underlying trauma. Treatment helps many people

who have PTSD understand the source of their symptoms and accept the circumstances of what happened to them, though for others the trauma is too great and symptoms are difficult to manage.

Risk Factors and Preventive Measures

Anyone who experiences a traumatic event may develop PTSD. There are no measures to identify who is particularly susceptible or to prevent PTSD. Early detection and initiation of treatment help minimize the extent to which PTSD causes disruption in the person's life.

See also ACUTE STRESS DISORDER; BRIEF REACTIVE PSYCHOSIS.

psychosis Any of numerous psychiatric disorders in which there is a complete break with reality. A person who has a psychotic disorder commonly experiences DELUSION (untrue belief) and HALLUCINATION (untrue sensory perception) and exhibits bizarre behavior in response. SCHIZOPHRENIA, MANIA, BIPOLAR DISORDER, DISSOCIATIVE DISORDER, OBSESSIVE–COMPULSIVE DISORDER (OCD), and personality disorders are among the more common psychoses. Often, components of multiple psychotic disorders coexist—that is, a person may have some symptoms of a dissociative disorder, some symptoms of OCD, and some symptoms of a personality disorder.

The diagnostic path is often complex and generally begins with a comprehensive NEUROLOGIC EXAMINATION to rule out organic causes (such as ALZHEIMER'S DISEASE or BRAIN TUMOR) that could cause the symptoms. Substance abuse and long-term ALCOHOLISM may also cause psychosis. Psychotic disorders require treatment with medications, often multiple medications in various combinations that attempt to manage the range of symptoms. PSYCHOTHERAPY in combination with medications is sometimes more effective, though this depends on the psychotic behaviors. Severe psychotic disorders require intensive treatment in an inpatient hospital setting. Psychotic disorders are often chronic and difficult to treat, though understanding of brain biochemistry continues to evolve and result in new types of medications.

See also ANTIANXIETY MEDICATIONS; ANTIDEPRESSANT MEDICATIONS; ANTIPSYCHOTIC MEDICATIONS; NEUROSIS; PARANOIA.

psychotherapy A collective term for the dozens of treatment approaches based on interaction and dialogue between a person and a mental health professional (therapist, psychologist, psychiatrist). Pure psychotherapy does not involve the use of medications; however, many people who are in psychotherapy also take medications to mitigate the symptoms of their conditions. Because many psychiatric disorders and psychologic conditions involve deeply rooted and complex issues, psychotherapy tends to extend over months to years. Some therapies specifically target narrow issues for rapid results, such as BEHAVIOR MODIFICATION THERAPY and COGNITIVE THERAPY. The success of psychotherapy depends on many factors.

See also ELECTROCONVULSIVE THERAPY (ECT).

S–T

seasonal affective disorder (SAD) DEPRESSION that develops during the winter months when the hours of darkness exceed the hours of daylight. Researchers believe a key factor in SAD is an increase in the amount of MELATONIN the PITUITARY GLAND produces. Melatonin is a HORMONE that regulates the body's circadian cycle (wake and sleep pattern). Darkness stimulates melatonin release. Higher than normal levels of melatonin cause tiredness and reduce energy. Bright light causes the pituitary gland to back off melatonin production, causing wakefulness and alertness. Another factor may be the level of serotonin, a NEUROTRANSMITTER associated with mood, in the BRAIN.

Symptoms of SAD commonly appear each year during the winter months and include

- profound lethargy
- disinterest in life
- tiredness or urge to sleep
- craving for sweets (simple carbohydrates)
- weight gain

The most effective treatment for SAD is exposure to bright light, ideally sunlight outdoors. Walking an hour a day in the winter often dramatically improves symptoms, likely a combination effect of the exposure to light and exercise. Arranging one's workspace to have as much natural light as possible (or using light bulbs that emulate daylight) is often helpful for people who cannot get outdoors during daylight hours. Symptoms cause significant enough dysfunction in some people to warrant therapy with ANTIDEPRESSANT MEDICATIONS, typically selective serotonin reuptake inhibitors (SSRIs) to increase serotonin levels in the brain.

See also EXERCISE AND HEALTH RISK REDUCTION; POSTPARTUM DEPRESSION; SLEEP DISORDERS; WALKING FOR FITNESS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

schizophrenia A serious psychotic disorder with marked emotional, cognitive, and physical symptoms. Schizophrenia represents a profound and disabling break from reality. Researchers do not know what causes schizophrenia, though it tends to run in families, which suggests a genetic foundation is likely. Differences in BRAIN structure in people who have schizophrenia, apparent with diagnostic imaging, also suggest organic factors that likely affect the ways the brain receives, organizes, and processes information. Symptoms in men often begin in late ADOLESCENCE or early adulthood; symptoms in women tend to develop in early to middle adulthood. More than three million Americans have schizophrenia.

Symptoms and Diagnostic Path

There are five types of schizophrenia—catatonic, disorganized, paranoid, undifferentiated, and residual—that share many common symptoms as well as have unique symptoms. These symptoms must be continuous six months or longer and represent a dramatic and observable deterioration in function. Symptoms common to all types of schizophrenia, though present to differing degrees in different types, include

- DELUSION (untrue belief)
- HALLUCINATION (false sensory perception)
- chaotic or disordered thought processes and expression of ideas
- bizarre behavior and involuntary movement

- lack of emotional response or demeanor (flat affect)

The diagnostic path often includes COMPUTED TOMOGRAPHY (CT) SCAN or MAGNETIC RESONANCE IMAGING (MRI) of the head to rule out physical causes, such as BRAIN TUMOR, for symptoms. Diagnosis is sometimes difficult because symptoms are similar to those of other psychotic disorders. There are no conclusive diagnostic procedures, and psychiatrists sometimes differ in their clinical opinions as to whether a person has schizophrenia or another psychotic disorder. However, treatment approaches are usually the same, at least initially.

Treatment Options and Outlook

Schizophrenia requires treatment with ANTIPSYCHOTIC MEDICATIONS to moderate and mitigate symptoms. Though these medications have significant side effects, they often restore the ability to interact in the world. Most people require several medications to adequately cover all symptoms. The balance of medication, both DRUG and dosage, is often a trial-and-error process as each person responds in a unique way to a particular medication as well as to combinations of medications. However, many people who have schizophrenia are able to work and engage in personal and social relationships once medications control their symptoms.

People who have schizophrenia are at increased risk for suicide, a risk that is most significant when treatment moderates symptoms and the person begins to reengage with normal life. It is common for DEPRESSION to emerge at this time. Psychiatrists often incorporate ANTIDEPRESSANT MEDICATIONS into the treatment regimen to offset this development.

Schizophrenia is a chronic disorder that requires lifelong, consistent treatment. Though it is essential for the person to continue medications as prescribed, many people fail to do so for various reasons. Some medications to treat schizophrenia are expensive, and all have potentially significant side effects that can make them unpleasant to take. Inherent in most forms of schizophrenia is distrust of others, a characteristic particularly prominent in paranoid schizophrenia. This distrust may combine with PARANOIA to cause the person to believe the medications are poisonous and refuse to take them. Further supporting this distrust is the sometimes necessary step of involuntary hospitalization to treat severe symptoms, notably when the person becomes a threat to self or others. Inconsistency in complying with medication regimens results in relapses of symptoms.

Risk Factors and Preventive Measures

The only known risk factor for schizophrenia is family history, though researchers do not know the basis of the genetic connections. Most people who have schizophrenia have no known family history of the disorder. There are no measures to prevent schizophrenia.

See also DISSOCIATIVE DISORDER; NEUROSIS; PERSONALITY DISORDER; PSYCHOSIS.

sleep disorders Disturbances of normal sleep patterns. Though there are dozens of types of sleep disorders, they fall into three general categories: insufficient sleep, disrupted sleep, and excessive or inappropriate sleep.

The body requires adequate sleep to restore cellular functions throughout the body. The BRAIN is active on different levels during sleep than when awake. Dreaming is particularly important for restful sleep. Though the amount of sleep needed varies among individuals as well as with age, everyone needs a consistent amount and quality of sleep most nights of the week.

Sleep disturbances, and in particular sleep deprivation, most significantly affect the NERVOUS SYSTEM, altering cognitive function and memory as well as motor function, balance, spatial orientation, and coordination. Public health experts estimate that sleep deprivation causes more MOTOR VEHICLE ACCIDENTS than intoxication and more work-related injuries than any other single cause. Sleepy drivers are often unaware of the extent to which their drowsiness impairs judgment and reaction time. More than 40 million Americans have chronic sleep disorders.

Symptoms and Diagnostic Path

The symptoms of inadequate sleep include

- daytime tiredness
- inability to concentrate or remember simple directions

- irresistible urge to nap
- drowsiness when driving or engaged in repetitious activity
- excessive snoring (OBSTRUCTIVE SLEEP APNEA) or moving around (RESTLESS LEGS SYNDROME)

The diagnostic path begins with a comprehensive medical examination to rule out physical causes or health conditions, particularly obstructive sleep apnea. Evaluation in a sleep lab allows observation of sleep patterns (polysomnography study). The person may spend one to five nights in the sleep lab, depending on the suspected causes of sleep disturbances, during which technicians observe, videotape, and record vital information such as HEART RATE, BLOOD PRESSURE, and electrical activity in the brain. ELECTROENCEPHALOGRAM (EEG) while awake and while asleep can detect subclinical SEIZURE DISORDERS or other abnormalities of the brain's electrical activity that may interfere with sleep.

Treatment Options and Outlook

Lifestyle measures are often successful in improving the amount and quality of restful sleep. One of the most important is going to bed at the same time every night, which helps the body establish a conscious rhythm of slowing down as that time approaches. Other lifestyle approaches to improve sleep include

- avoiding heavy meals, CAFFEINE, ALCOHOL, and tobacco within four hours of bedtime
- establishing quiet and darkness in the bedroom, even if a daytime sleeper because of night shift work
- getting 20 to 30 minutes of physical exercise, preferably outdoors, every day

Over-the-counter sleep aids often contain ANTIHISTAMINE MEDICATIONS, which induce sleep. Prescription sleep aids are often sedatives. Though sleep aids are effective for occasional use, over the long term they are more likely to interfere with sleep than improve its quality. Most medications that induce sleep affect neuroreceptors in the brain, which alters the way the brain functions during sleep. The sleep aid may induce sleep but prevent REM sleep and the dreams that occur during it, reducing the restful quality of the sleep.

MELATONIN supplementation can sometimes help readjust the body's rhythms to encourage sleep during daylight hours, particularly for night shift workers. Melatonin is a HORMONE the PITUITARY GLAND produces on a cyclic basis that initiates sensations of drowsiness when it is time to sleep. Warm chamomile tea, warm baths, or reading for 10 to 20 minutes before going to bed also may help the transition from the activities of the day to the calm that precedes restful sleep. Self-HYPNOSIS, relaxation techniques or audiotapes, and BIOFEEDBACK are other methods to prepare for sleep.

TO NAP OR NOT TO NAP

For many people who do not get enough sleep, the urge to nap during the day is irresistible. Though napping often provides a boost of energy and alertness in the short term, in the long term it can contribute to sleep disturbances such as insomnia.

Risk Factors and Preventive Measures

People who work night shifts and sleep during the day, which is counter to the body's natural circadian rhythm (cycle of sleep and wake), are most likely to have sleep disorders. Sleep disorders may result from physical conditions, such as obstructive sleep apnea or CHRONIC PAIN, as well as from neurologic disorders that affect BREATHING or MUSCLE control. OBESITY is the primary cause of obstructive sleep apnea. Sleep disturbances are common in many chronic health conditions, both physical and psychologic. These factors are often difficult for people to change. Other factors that influence sleep are alcohol and tobacco use, EATING HABITS and exercise patterns, and external environment (quiet or noisy, bright or dark). These are factors people can usually alter to improve the potential for sleep, once they become aware of the effects on sleep.

See also NARCOLEPSY.

somatization disorder Chronic perception of multiple illnesses and ailments for which doctors can find no clinical evidence. Stress often exacerbates symptoms. Because the physical complaints could indicate potentially serious illness, the most

common health-care response is to subject the person to comprehensive diagnostic testing. However, test results persistently produce no apparent physiologic cause for the symptoms. The person may go from one doctor to another, seeking diagnosis and treatment for symptoms that are all too real to the person regardless of the findings of diagnostic tests, causing the person to remain convinced he or she is seriously ill.

CHRONIC PHYSICAL SYMPTOMS COMMON IN SOMATIZATION DISORDER

abdominal pain and bloating	BACK PAIN
CHEST PAIN	DIARRHEA
difficulty BREATHING (DYSPNEA)	dizziness
DYSMENORRHEA	ERECTILE DYSFUNCTION
HEADACHE	JOINT PAIN
MUSCLE weakness	NAUSEA
PALPITATIONS	SEXUAL DYSFUNCTION
swallowing difficulty	VOMITING

Researchers do not fully understand what causes somatization disorder, though some of its mechanisms are clear and occur in other psychiatric conditions such as BODY DYSMORPHIC DISODER and GENERALIZED ANXIETY DISORDER (GAD). Some doctors may perceive the person is making himself or herself sick (FACTITIOUS DISORDERS). Recent research is uncovering new information about the integration among immune functions, neurologic functions, and psychologic functions (the field of PSYCHONEUROIMMUNOLOGY) that may reveal how these body systems affect the functions of each other in ways that shed light on conditions such as somatization disorder.

Diagnosis of somatization disorder is often difficult because the symptoms are real (the person experiences them, even though there are no apparent causes) and because many people see multiple doctors in their searches for answers. Consistent care from the same health-care provider is the most effective means for detecting and diagnosing somatization disorder.

Though psychiatric treatment or counseling could help many people understand the psychologic and emotional components to their symptoms, another function of the disorder is the flat refusal to acknowledge these components are present. In many situations the person may experience side effects or complications as a result of invasive diagnostic procedures and even surgeries. Noninvasive treatments such as BIOFEEDBACK, ACUPUNCTURE, and VISUALIZATION are often helpful for people who have somatization disorder just as they are for people who have similar symptoms with identifiable physiologic causes. People who can gain insight into the health relationship between body and mind and who can use these body–mind methods are often able to satisfactorily control their symptoms for long-term relief.

See also CHRONIC FATIGUE SYNDROME; CONVERSION DISORDER; FIBROMYALGIA; HYPOCHONDRIASIS; MIND–BODY INTERACTIONS; STRESS AND STRESS MANAGEMENT.

suicidal ideation and suicide Thoughts of killing oneself, attempting to kill oneself, or succeeding in killing oneself. The risk for suicide is highest among people who have DISSOCIATIVE DISORDER, clinical DEPRESSION (major depression), SCHIZOPHRENIA, and BIPOLAR DISORDER. Substance abuse and ALCOHOLISM are also risk factors. Stressful life events and circumstances heighten the risk and may serve as precipitating factors. People who have degenerative or debilitating physical health conditions may also contemplate or attempt suicide.

It is important to take seriously any comments a person makes about taking his or her life, and to encourage the person to seek help. Most communities have suicide hot lines or crisis intervention services.

Suicide is intensely traumatic and very difficult to understand for family members and friends. Though occasional thoughts of suicide are common and most people who talk about death or suicide make no attempts to take their own lives, many people who carry through with suicide give some indications (though sometimes subtle) that suicide is at least in their thoughts. Suicide among men is more likely to involve firearms or hanging; suicide among women is more likely to result from medication OVERDOSE. Loved ones often feel responsible and guilty for missing the clues.

A common misunderstanding about suicide is that discussing it encourages it. In most situations,

the reverse is more true. Many people are relieved to be able to discuss their fears and worries and are receptive to less drastic solutions that perhaps previously had not occurred to them. All states in the United States provide for involuntary hospitalization of people who present clear danger to themselves, though most have stringent criteria for determining whether such hospitalization is appropriate. Other preventive measures include appropriate treatment for the underlying psychologic condition or psychiatric disorder and close supervision or monitoring.

See also END OF LIFE CONCERNS; STRESS AND STRESS MANAGEMENT.

trichotillomania Compulsively pulling out one's HAIR such that hair loss occurs and is obvious. Pulling the hair results in a sense of relief from stress or anxiety. Trichotillomania often begins in early ADOLESCENCE and is more common in girls. There is commonly a precipitating event that is stressful or traumatic, though some research suggests the fluctuating hormonal environment within the body during PUBERTY may trigger the condition. Some psychiatrists believe trichotillomania is a form of OBSESSIVE–COMPULSIVE DISORDER (OCD) because many people who have trichotillomania also engage in some degree of compulsive behavior such as counting rituals or repetitiously washing the hands. As well, the current therapeutic approach for trichotillomania is treatment with a combination of BEHAVIOR MODIFICATION THERAPY and medications such selective serotonin reuptake inhibitors (SSRIs) and the antiseizure medication valproate. These are the same medications used to treat OCD. People who are successful in changing their behavior often experience long-term relief, although the trichotillomania may return in times of intense stress.

COMMON MEDICATIONS TO TREAT TRICHOTILLOMANIA	
clomipramine	fluoxetine
lithium carbonate	paroxetine
sertraline	valproate

See also ALOPECIA; ANTIDEPRESSANT MEDICATIONS; DEPRESSION; GENERALIZED ANXIETY DISORDER (GAD); STRESS AND STRESS MANAGEMENT.

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VOLUME 4

FOREWORD

A big part of my role as a physician is educating my patients about their health. I take as much time as each person needs to explain prevention measures, test results, and treatment options. I encourage questions. But in the moment, sitting there in my office, most people do not yet know what to ask me. By the time questions flood their thoughts, they may be back at work or at home.

Numerous events and circumstances can challenge health, and we all need to know what actions we can take to keep ourselves healthy as well as to obtain appropriate treatment for health conditions that do affect us. Knowledge empowers all of us to make informed and appropriate decisions about health care. Certainly there is no shortage of reference material. Yet there is *so* much information available today! Even for physicians, it is challenging to keep up. How can you get to the core of what you want to know, reliably and to the level of detail you need?

The Facts On File Encyclopedia of Health and Medicine is a great resource for up-to-date health information presented in a manner that is both comprehensive and easy to understand no matter what your level of medical knowledge. The encyclopedia organizes entries by body system. The progression of body systems—and entries—throughout the encyclopedia presents topics the way you think about them.

Going beyond this basic structure, however, is another layer of organization that particularly appeals to me, which is a comprehensive structure of cross references that integrates entries across body systems. After all, your body functions in an integrated way; so, too, should a reference series that discusses your body's health. Not very much that happens with your health affects one part of your body in isolation from other body structures and functions. Your body attempts to compensate and adjust, often without your awareness, until it can no longer accommodate the injury or illness. The symptoms you bring to your doctor may reflect this compensation, for example frequent headaches that point not to brain tumor (as many people fear but is very rare) but to eye strain or muscle tension or sometimes to hypertension (high blood pressure).

In my medical practice I emphasize integrative health care, embracing the philosophy that health exists as the intricate intertwining of the body's many systems, structures, and functions. So, too, does the care of health. I received my medical degree from Tufts University School of Medicine in Boston, an institution noted for remaining at the forefront of the medical profession. I also completed clinical programs in Mind-Body Medicine at Harvard University, Integrative Medicine at the University of Arizona School of Medicine, and Medical Acupuncture at the University of California-Los Angeles (UCLA). I am a board-certified obstetrician-gynecologist, a board-certified clinical nutritionist, and a licensed acupuncturist. I see patients in my practice in Cincinnati, Ohio; I teach, I lecture, and I frequently go on television and radio to talk about health topics. In each of these areas, I encourage people to think about their health and health concerns from an integrative perspective. When you understand your health from multiple dimensions, you can better understand what to do to keep yourself as healthy as possible.

I wish you the best of health for all of a long, satisfying life. But when the time comes that you must make decisions about medical care, I want you to have the knowledge to make informed

choices that are right for you. Whether you start here and move on to more specialized resources or locate all the information you need within these four volumes, you will find *The Facts On File Encyclopedia of Health and Medicine* to be a most valuable reference resource.

—Maureen M. Pelletier, M.D., C.C.N., F.A.C.O.G.

HOW TO USE
THE FACTS ON FILE ENCYCLOPEDIA OF HEALTH AND MEDICINE

Welcome to *The Facts On File Encyclopedia of Health and Medicine*, a four-volume reference set. This comprehensive resource is an indispensable reference for students, allied health professionals, physicians, caregivers, lay researchers, and people seeking information about health circumstances and conditions for themselves or others. Entries present the latest health concepts and medical knowledge in a clear, concise format. Readers may easily accumulate information and build a complete medical profile on just about any health or medical topic of interest or concern.

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As the art and science of health and medicine continues to evolve, with complex and elegant discoveries and new techniques, medications, and treatments emerging all the time, the need has arisen for a new paradigm for the encyclopedia of health and medicine—a rethinking of the old, and increasingly outmoded, presentations. Carefully researched and compiled, *The Facts On File Encyclopedia of Health and Medicine* offers many distinguishing features that present readers and researchers with an organization as up-to-date and compelling as the breakthrough information its entries contain.

Recognizing the current emphasis on presenting a truly integrative approach to both health and disease, *The Facts On File Encyclopedia of Health and Medicine* organizes content across volumes within a distinctive format that groups related entries by body system (for example, "The Cardiovascular System") or by general health topic (for example, "Genetics and Molecular Medicine"):

- **Volume 1** presents the sensory and structural body systems that allow the body to engage with its surroundings and the external environment.
- **Volume 2** presents the cell- and fluid-based body systems that transport nutrients, remove molecular wastes, and provide protection from infection.
- **Volume 3** presents the biochemical body systems that support cellular functions.
- **Volume 4** presents topics that apply across body systems (such as "Fitness: Exercise and Health") or that address broad areas within health care (such as "Preventive Medicine").
- The appendixes provide supportive or additional reference information (such as "Appendix X: Immunization and Routine Examination Schedules").

Following Research Pathways

The Facts On File Encyclopedia of Health and Medicine's organization and structure support the reader's and researcher's ease of use. Many encyclopedia users will find all the information they desire within one volume. Others may use several or all four of the encyclopedia's volumes to arrive at a comprehensive, multifaceted, in-depth understanding of related health and medical concepts and information. Researchers efficiently look up information in *The Facts On File Encyclopedia of Health and Medicine* in several ways.

Each section's entries appear in alphabetical order (except the entries in Volume 4's "Emergency and First Aid" section, which are grouped by type of emergency). The researcher finds a desired entry by looking in the relevant volume and section. For example, the entry for **acne** is in Volume 1 in the section "The Integumentary System" and the entry for **stomach** is in Volume 3 in

the section "The Gastrointestinal System." The researcher can also consult the index at the back of the volume to locate the entry, then turn to the appropriate page in the volume.

Terms that appear in SMALL CAPS within the text of an entry are themselves entries elsewhere in *The Facts On File Encyclopedia of Health and Medicine*. Encyclopedia users can look up the entries for those terms as well, for further information of potential interest. Such SMALL CAPS cross references typically provide related content that expands upon the primary topic, sometimes leading the user in new research directions he or she might otherwise not have explored.

For example, the entry **hypertension** is in the section "The Cardiovascular System." The entry presents a comprehensive discussion of the health condition hypertension (high blood pressure), covering symptoms, diagnosis, treatment options, risk factors, and prevention efforts. Among the numerous SMALL CAPS cross references within the hypertension entry are the entries for

- **retinopathy**, an entry in the section "The Eyes" in Volume 1, which discusses damage to the eye that may result from untreated or poorly managed hypertension
- **blood pressure**, an entry in the Volume 2 section "The Cardiovascular System," which discusses the body's mechanisms for maintaining appropriate pressure within the circulatory system
- **stroke** and **heart attack**, entries in Volume 2's "The Cardiovascular System" about significant health conditions that may result from hypertension
- **kidney,** an entry in the section "The Urinary System" in Volume 3, which discusses the kidney's role in regulating the body's electrolyte balances and fluid volume to control blood pressure
- **atherosclerosis, diabetes, hyperlipidemia,** and **obesity**, entries in the sections "The Cardiovascular System" in Volume 2, "The Endocrine System" in Volume 3, and "Lifestyle Variables: Smoking and Obesity" in Volume 4, and all of which are health conditions that contribute to hypertension

Following the path of an encyclopedic entry's internal cross references, as shown above, can illuminate connections between body systems; define and apply medical terminology; reveal a broad matrix of related health conditions, issues, and concerns; and more. The SMALL CAPS cross references indicated within the text of encyclopedic entries lead encyclopedia users on wide-ranging research pathways that branch and blossom.

At the end of the entry for **hypertension** a list of cross references gathered in alphabetical order links together groups of related entries in other sections and volumes, such as **smoking cessation** in Volume 4's "Lifestyle Variables: Smoking and Obesity," to provide specific, highly relevant research strings. These *see also* cross references also appear in SMALL CAPS, identifying them at a glance. Encyclopedia users are encouraged to look here for leads on honing research with precision to a direct pathway of connected entries.

So, extensive cross-references in *The Facts On File Encyclopedia of Health and Medicine* link related topics within and across sections and volumes, in both broad and narrow research pathways. This approach encourages researchers to investigate beyond the conventional level and focus of information, providing logical direction to relevant subjects. Each cross-referenced entry correspondingly has its own set of cross references, ever widening the web of knowledge.

Using the Facts On File Encyclopedia of Health and Medicine

Each section of the encyclopedia begins with an overview that introduces the section and its key concepts, connecting information to present a comprehensive view of the relevant system of the human body or health and medical subject area. For most body systems, this overview begins with a list and drawings of the system's structures and incorporates discussion of historic, current, and future contexts.

Entries present a spectrum of information from lifestyle factors and complementary methods to the most current technologic advances and approaches, as appropriate. Text that is set apart or bold within an entry gives an important health warning, or targets salient points of interest to add layers of meaning and context. Lists and tables

collect concise presentations of related information for easy reference.

Each type of entry (mid-length and longer) incorporates consistent elements, identified by standardized subheadings:

- ***Entries for health conditions and diseases*** begin with a general discussion of the condition and its known or possible causes and then incorporate content under the subheadings "Symptoms and Diagnostic Path," "Treatment Options and Outlook," and "Risk Factors and Preventive Measures."
- ***Entries for surgery operations*** begin with a general discussion of the procedure and then incorporate content under the subheadings "Surgical Procedure," "Risks and Complications," and "Outlook and Lifestyle Modifications."
- ***Entries for medication classifications*** begin with a general discussion of the type of medication and its common uses and then incorporate content under the subheadings "How These Medications Work," "Therapeutic Applications," and "Risks and Side Effects."
- ***Entries for diagnostic procedures*** begin with a general discussion of the test or procedure and then incorporate content under the subheadings "Reasons for Doing This Test," "Preparation, Procedure, and Recovery," and "Risks and Complications."

Entries in Volume 4's section "Emergency and First Aid" are unique within the orientation of *The Facts On File Encyclopedia of Health and Medicine* in that they feature instructional rather than informational content. **These entries do *not* replace appropriate training in emergency response and first aid methods.** Rather, these entries provide brief directives that are appropriate for guiding the actions of a person with little or no first aid training who is first on the scene of an emergency.

Each volume concludes with a complete, full index for the sections and entries within the volume. Volume 4 of *The Facts On File Encyclopedia of Medicine* contains a comprehensive index for all four encyclopedia volumes that researchers can use to quickly and easily determine which volumes contain desired sections or entries.

The Facts On File Encyclopedia of Health and Medicine in Four Volumes

PREFACE TO VOLUME 4

Volume 4 of the four-volume *The Facts On File Encyclopedia of Health and Medicine* is unique in its organization and presentation of content. The sections of Volume 4 extend across body systems and medical disciplines to look at the larger picture of health and health care. Though the entries in these sections cover a broad spectrum of information, the thread that connects all of these sections is the individual's participation, through lifestyle choices and informed decisions, in his or her health and health care.

Preventive Medicine

The protection of a population's overall health, particularly measures to maintain health and prevent health problems, is a major emphasis. The section "Preventive Medicine" examines efforts and initiatives intended to reduce the general risks for injury or illness. Entries present both personal and community-based perspectives.

Alternative and Complementary Approaches

The section, "Alternative and Complementary Approaches" explores methods based in other systems of health care such as acupuncture and herbal remedies. Entries present the methods within the framework of how they fit within the Western medicine model common in the United States, with cross references to comparable Western approaches discusses in entries elsewhere in *The Facts On File Encyclopedia of Health and Medicine*.

Genetics and Molecular Medicine

In April 2003 an international, cross-disciplinary team of scientists completed the human genome sequence, unraveling for the first time the structure of human existence. The section "Genetics and Molecular Medicine" entries look at research that uses the map of the human genome to explore new pathways for understanding disease and illness. Through this new knowledge lies hope for preventing many of the health conditions common today.

Drugs

Pharmaceutical therapies are the basis for treatment of many health conditions, from infections to cardiovascular disease to cancer. The section "Drugs" contains entries that discuss the types of medications doctors use to treat a wide range of health conditions. Entries cover classifications of prescription drugs as well as over-the-counter products and include cross references to alternative remedies.

Nutrition and Diet

Nutrition (what the body requires to fuel its functions) comes from diet (the foods people eat). Dietary choices affect nutrition, and consequently health, in ways that can support health and lower the risk for disease. The entries in this section discuss the major categories of nutrients and explain how dietary choices affect the body's functions.

Fitness: Exercise and Health

Fitness reflects a personal choice to engage in activities that maintain the body's strength, flexibility, and mobility to support optimal health. Many researchers consider physical *in*activity to be the leading factor in the development of chronic health conditions such as hypertension (high blood pressure), diabetes, and obesity. The entries in this section discuss the correlation between regular physical activity and key health conditions as well as present information about how physical activity affects the body.

Human Relations

Humans are social beings. Yet many social interactions are ones not necessarily chosen, such those within school and work environments. The entries here present discussions of behavior issues, with an emphasis on understanding the influence of diverse backgrounds and personal experiences.

Surgery

Surgery is the treatment of choice for hundreds of health conditions. The section "Surgery" presents entries about general topics such as anesthesia and surgery benefits and risks. Entries about specific operations appear in the relevant body system section. For example, the entry for appendectomy (surgery to remove the appendix) appears in the section "The Gastrointestinal System."

Lifestyle Variables: Smoking and Obesity

Cigarette smoking and obesity (extreme overweight) are the leading lifestyle factors that contribute to serious health conditions such as cardiovascular disease, diabetes, and cancer. In this section *The Facts On File Encyclopedia of Health and Medicine* presents entries about the health effects of smoking and obesity within the context of lifestyle choices that are within the reach of every individual to control.

Substance Abuse

Substance abuse, including alcoholism, is a significant health concern in the United States. The entries in this section discuss commonly abused substances, including their short-term and long-term effects on health. There are also entries about treatment approaches and programs.

Emergency and First Aid

The section "Emergency and First Aid" stands apart from all other sections in the *Facts On File Encyclopedia of Health and Medicine.* Entries here provide instructional content and are organized by type of emergency, presenting the most basic information for the person who has no medical knowledge or training and who happens to be first on the scene of a medical emergency (first responder). Entries are concise and directive, with cross references to information-based entries throughout the four volumes of the encyclopedia.

Appendixes and Cumulative Index to Volumes 1-4

A dozen appendixes that provide supplemental information bring Volume 4 to a close. Volume 4 also contains a comprehensive "Cumulative Index" for the entire four-volume *Facts On File Encyclopedia of Health and Medicine*.

PREVENTIVE MEDICINE

The medical discipline of preventive medicine covers the gamut of measures, individual and societal, that can reduce the occurrence of illness and injury. Physicians who practice in preventive medicine may be infectious disease specialists, community health specialists, and occupational health specialists. Preventive medicine is also a mainstay of most other medical specialties, notably family practice, internal medicine, and pediatrics. The research field of epidemiology studies trends in and risks for illness and injury and explores methods for reducing health risks. Epidemiologists and preventive medicine practitioners work closely together.

This section, "Preventive Medicine," presents an overview discussion of preventive medicine concepts and entries about preventive health measures and the public health dimensions of illness and injury. The entries in this section focus on the larger picture of how illness and injury affect the health and well-being of communities and populations. Entries in other sections of *The Facts On File Encyclopedia of Health and Medicine* provide detailed content about the causes, symptoms, diagnosis, treatment, and outlook for specific infections and diseases. Cross-references link the entries to one another.

Traditions in Preventive Medicine History

Early cultures and medical systems had their unique variations on preventing illness and INFECTION. There is some evidence of guidelines for sanitation and public health practices in ancient Macedonia, and the ruins of ancient Rome's intricate aqueducts and sewage canals remain today. But for the most part the premise of public health is relatively modern, emerging after a flurry of scientific discoveries in the 19th century that revealed the pathogenesis (origin and progression) of infection and disease. Key to these discoveries were the observations of physicians such as Ignaz Philipp Semmelweis, who was the first to make the connection that doctors carried the infection of childbirth FEVER from one patient to another through blood on their hands and clothing, and the experiments of scientists such as Joseph Lister, Louis Pasteur, and Robert Koch, whose discoveries proved the existence of microbes and the value of antisepsis in preventing the spread of infection. Their work further led to the development of antibiotics and vaccines.

These three factors—antisepsis, antibiotics, and vaccines—forever changed the perceptions and patterns of disease throughout the world and are among the most significant breakthroughs in medical history. In less than half a century these discoveries dramatically reduced the occurrence and severity of many diseases that had for millennia been the leading causes of death: tetanus, ANTHRAX, SMALLPOX, CHOLERA, TYPHOID FEVER, DIPHTHERIA, PERTUSSIS, POLIOMYELITIS, SYPHILIS, bacterial PNEUMONIA, bacterial wound infections, INFLUENZA, and TUBERCULOSIS. Though death due to infection after CHILDBIRTH is rare in the United States today, until the early 20th century childbirth fever (puerperal fever) was a leading cause of death among women of childbearing age. From 1900 to 1999, maternal death in childbirth declined 99 percent in the United States.

EFFECTS OF VACCINATION

- eradication of SMALLPOX in the United States in 1967 and worldwide in 1977
- near eradication of MEASLES in the United States in 1998
- near eradication of POLIOMYELITIS in the United States in 2000

Public Health

Improvements in COMMUNITY SANITATION, such as sewage and garbage control, in the late 19th and early 20th centuries further contained diseases spread through close contact reduced pest and vermin infestation and the resultant diseases, including the much dreaded "black death," plague. Cities and towns focused effort on maintaining clean and safe drinking water supplies, decreasing waterborne illnesses. The home refrigerator debuted in 1913 and quickly replaced the icebox as the standard for food storage, dramatically decreasing FOODBORNE ILLNESSES.

Doctors and others began to recognize, by the start of the 20th century, the extent to which community and personal cleanliness influenced health and illness. Poor ventilation and overcrowded living and working conditions, especially in densely populated cities, encouraged rampant and rapid spread of infectious diseases. In 1900 pneumonia, tuberculosis, and GASTROENTERITIS together were to blame for a third of all deaths in the United States. Annual influenza outbreaks could kill entire families, even communities, within weeks. In cities, infections caused the deaths of nearly a third of infants before their first birthdays.

With clean water standards came assurances that bathing would no longer be the source of illness but rather could be the guardian of health. Public officials began to extol the virtues of frequent HAND WASHING and daily, or at least weekly, bathing. Between 1920 and 1937 illnesses and deaths from waterborne infections such as cholera and typhoid fever plummeted, and by 1950 were nearly nonexistent. Health officials also encouraged opening windows and getting fresh air, measures that helped dilute the concentration of airborne pathogens such as viruses and BACTERIA and reduce opportunities for infection to occur. In 1944 the US Congress passed the Public Health Service Act that established a consistent framework for public health laws, standards, and procedures throughout the United States.

Life expectancy A key measure of public health and the effectiveness of disease-prevention efforts is LIFE EXPECTANCY. A child born in 1900 could expect to live to age 47. A child born in 1950, the dawn of the golden era of preventive health care, could expect to live nearly half again as long, to age 68. These children were the first who also could expect to grow up without experiencing the CHILDHOOD DISEASES that claimed the lives of one in five children in their parents' generation.

Epidemics and pandemics Epidemics and pandemics strike fear in the hearts of health experts and individuals alike. Epidemics are extensive but localized outbreaks of illness or infection. Pandemics are worldwide outbreaks. Despite vaccination efforts, annual influenza epidemics sicken millions and cause the deaths of 30,000 Americans. Health experts believe basic preventive measures such as frequent hand washing and appropriate SNEEZE/COUGH ETIQUETTE, combined with more comprehensive vaccination, could prevent most of these infections.

The Spanish influenza epidemic of 1918, the worst pandemic of modern history, claimed the lives of half a million Americans and more than 20 million people worldwide. It also provided much learning for public health officials about how, and how quickly, such infections spread. Health experts have used this knowledge to develop mechanisms and systems to detect and report outbreaks that have pandemic potential. Such efforts could not entirely prevent, though did help contain, influenza pandemics in 1957 (the Asian flu) and 1968 (the Hong Kong flu). They did, however, allow early detection and containment of small outbreaks of avian influenza in 2000 and 2004, and of the deadly SEVERE ACUTE RESPIRATORY SYNDROME (SARS).

Motor vehicle safety A uniquely modern-day public health issue is motor vehicle safety. Coming into its own in the early 1900s, the automobile wasted little time acquiring notoriety. By the time Henry Ford set the standard for the "everyman" car, MOTOR VEHICLE ACCIDENTS had already claimed more than 40,000 lives. By the 1960s, motor vehicle accidents accounted for more than 40,000 deaths each year. Measures such as structural integrity requirements, seat belts, and airbags have held motor vehicle deaths steady near that level since 1998.

Individual Health Factors

The recognition that PERSONAL HYGIENE—frequent hand washing and daily or at least weekly bathing—could prevent the passing of disease from one person to another was a milestone in

preventive medicine. Until the early 20th century even doctors did not often wash their hands, not even between seeing patients. This was largely a function of ignorance. Until Lister, Koch, Pasteur, and others demonstrated the existence of bacteria and their causal relationship to infection, doctors and others simply did not know their hands carried the agents of disease. Health experts today believe that frequent hand washing could prevent 90 percent or more of the infections that occur.

THE US CENTERS FOR DISEASE CONTROL AND PREVENTION'S (CDC'S) 10 MOST SIGNIFICANT PUBLIC HEALTH ACHIEVEMENTS OF THE 20TH CENTURY

control of infectious diseases
decline in deaths from heart disease and STROKE
FAMILY PLANNING
FLUORIDATION of drinking water
healthier mothers and babies
motor-vehicle safety
recognition of TOBACCO use as a health hazard
safer and healthier foods
safer workplaces
vaccination

Source: CDC, MMRW Weekly, April 2,1999, 48(12):241–243.

Health discoveries in the 1950s and 1960s began to connect lifestyle habits with health and disease. The landmark surgeon general's report of 1964 established the scientific correlation between cigarette smoking and LUNG disease, notably lung CANCER. Research explored the roles of nutrition and exercise in preventing disease and even in the early 1960s issued recommendations for daily "calisthenics" to maintain the physical health of the body. Fast food (available in restaurants and from grocery stores) changed EATING HABITS and body weight, and health experts noted alarming rises in CARDIOVASCULAR DISEASE (CVD) and type 2 DIABETES.

In 1900 heart disease was the fourth leading cause of death in the United States; by 1977 it had become, and today remains, number one. Though infections such as HIV/AIDS and HEPATITIS remain significant threats to personal and public health, the greatest challenges are now those that are nearly exclusively within the realm of individual control. Health promotion emphasizes community-based as well as individual preventive efforts that target modifiable risk factors for injury, illness, and disease. Recommendations for individual preventive health measures emphasize nutritious eating habits and daily exercise, urge SMOKING CESSATION, promote IMMUNIZATION, and encourage routine health screenings for early detection and treatment of disease. Health experts believe lifestyle modifications—reduction of personal health risks—could eliminate as much as 90 percent of acquired heart disease as well as 95 percent of type 2 diabetes (a leading cause of heart disease).

KEY PERSONAL HEALTH FACTORS

ALCOHOL use
EATING HABITS
physical inactivity
safer sex practices
substance abuse
cigarette smoking
occupational and recreational safety
seat belt and helmet use

Contemporary Issues and Challenges

Preventive medicine specialists acknowledge the many challenges of controlling or eliminating the factors that result in the health conditions that are most significant at present. Despite the truly phenomenal strides in health care that have occurred in the past 50 years, the emphasis within the American health-care structure remains on treating disease. Factors that influence the success of prevention measures include cultural and generational perceptions, literacy and non-English-speaking populations, aging of the US population, access to care and mechanisms of care delivery, and disparities among population groups.

Cultural and generational perceptions Perceptions about health screening, preventive care, and even treatment for diagnosed health conditions differ among cultures and age groups. Older generations may hold to beliefs that one goes to the doctor only when ill or injured, stemming from limited access and affordability that typified health care before the emergence of health insurance. Ethnic groups may be suspicious of Western medicine and its intrusive nature or find conventional medical practices at odds with spiritual or religious beliefs. CULTURAL AND ETHNIC HEALTH-CARE PERSPECTIVES and GENERATIONAL HEALTH-CARE PERSPECTIVES greatly influence compliance with public health recommendations, affecting groups that are particularly vulnerable to health conditions, such as cardiovascular disease or infections such as hepatitis

and tuberculosis, that current preventive measures target.

Literacy A key platform of public health education efforts is the presentation of information through written materials such as posters, handout informational sheets, brochures, and display placards. Some studies suggest that up to two thirds of English-speaking individuals lack the functional literacy level to understand the content of these materials, complete health and risk assessment tools such as surveys and questionnaires, or follow written care instructions after procedures such as surgery. In regions where there are high concentrations of non-English-speaking populations, health education materials and basic health questionnaires are often available in the dominant languages of such populations. However, most people who do not understand materials the doctor gives them will not say so.

Aging of the US population In 1900, less than 4 percent of the American population—3 million people—was over the age of 65. In 2000, 35 million Americans, nearly 13 percent of the population, were age 65 and older, a 10-fold increase over the span of a century. By 2030 the US Bureau of the Census projects that 30 percent of the population—70 million people—will be over age 65. Given the rise in the frequency of health conditions such as cancer, cardiovascular disease, and diabetes as well as the conditions relatively specific to the older population such as ALZHEIMER'S DISEASE and PARKINSON'S DISEASE, the potential demand for health-care services may quadruple. Efforts to reduce the likelihood for preventable health conditions takes on increasing significance within this scenario.

Access to care and mechanisms of delivery Though 85 percent of Americans have private or public health insurance, 15 percent do not. In a delivery model predicated on insurance as primary payer, insurance coverage determines access to care. People who do not have health insurance have difficulty receiving health-care services and often are then more seriously ill when they do receive care. Health experts worry that lack of access to appropriate health-care services, including preventive measures such as immunization, increases the risk for outbreaks of infectious diseases. Of particular concern are SEXUALLY TRANSMITTED DISEASES (STDS), tuberculosis, hepatitis, and HIV/AIDS, all of which have significant public health ramifications.

Breakthrough Research and Treatment Advances

At the start of the 20th century doctors marveled at the notion that living organisms so small only the magnification of a microscope revealed their existence caused the many diseases that ravaged entire populations. Perhaps the most profound breakthrough in preventive medicine at the start of the 21st century is the mapping of the HUMAN GENOME. Within reach, and in various stages of research and development, are "smart" drugs that target specific substances in the body and pharmacogenomic products that will "turn off" predisposing genetic factors for diseases such as HYPERTENSION (high BLOOD PRESSURE), diabetes, and certain cancers. GENE THERAPY holds the promise of manipulations that may end diseases such as CYSTIC FIBROSIS.

No longer the venue of science fiction is the field of molecular medicine, in which doctors can redirect cell function. In 2001, after 10 years of intensive research, a multidisciplinary team of scientists finished decoding the human genome. The unprecedented achievement revealed startling and revolutionary insights into the functions of the human body. The offshoot Microbial Genome Program, initiated in 1994, continues to unravel the genetic encoding of the organisms that function at the most foundational level of organic existence. In the space of a century, medicine has come from identifying the existence of the MICROBE to understanding the most intimate details of its functions.

Yet even as technology ushers health care into the 21st century and beyond, the challenges of the previous century linger. Infectious illnesses, though different from those that plagued earlier generations, remain at the forefront of preventive medicine. The first Nobel Prize in Medicine or Physiology was awarded to Emil von Behring in 1901 for discovering the cause of one of the time's most deadly diseases, diphtheria. The 1997 award went to Stanley Prusiner for his discovery of another new pathogen, the infectious PRION. The most rampant infection in the world, HIV/AIDS, remains incurable. Preventive medicine is on a new, yet familiar, path as the current millennium moves forward.

A

accidental injuries Accidental injuries, also called unintentional injuries, claim more than 100,000 lives each year and are the fifth leading cause of death in the United States. Accidental injuries account for nearly half of childhood deaths. Accidental injuries further account for more than 90 million health-care provider (ambulatory medical care) visits annually, 10 million of which are for injuries to children. Many accidental injuries are preventable.

KEY PUBLIC HEALTH MEASURES TO REDUCE ACCIDENTAL INJURIES

boating safety regulations	building occupancy regulations
building sprinkler systems	child-resistant container laws
carbon monoxide detectors	fire codes
emergency exit requirements	flammability standards
fireworks restrictions	product labeling requirements
playground safety standards	smoke detectors
seat belt, child restraint, and helmet laws	structural building codes
traffic speed limits	vehicle safety standards

Major Causes of Accidental Injuries

There are numerous causes for accidental injuries. MOTOR VEHICLE ACCIDENTS lead them, accounting for 40 percent of those deaths. Poisoning and falls each account for 15 percent. Other common causes of accidental injuries include choking, fires, recreational activities, and fireworks.

Motor vehicle accidents Motor vehicle accidents are the leading cause of death for those between the ages of 2 and 33, resulting in more than 40,000 deaths each year. Motor vehicle accidents also account for nearly 3 million injuries for which people seek medical care each year. People between ages 15 and 25 years and over age 74 years are at highest risk for injury or death in motor vehicle accidents. The three most significant factors in motor vehicle accident injuries and deaths are:

- Improper restraints—nearly three fourths of those who die in motor vehicle accidents are not wearing seat belts or secured in child seats and are thrown from the vehicle in the accident.
- ALCOHOL use—alcohol use is involved in 40 percent of fatalities and 7 percent of accidents overall.
- Excessive speed—speeding contributes to a third of all motor vehicle accidents, though is a disproportionate factor among male drivers between the ages of 16 and 20.

Up to a third of motor vehicle accidents involve combinations of these factors, greatly increasing the likelihood of injury or death.

Poisoning Accidental poisoning accounts for 14,500 deaths and 500,000 injuries that require medical attention each year. More than 60 percent of poisonings are among children under the age of 14. Children under the age of 4 account for two thirds of poisonings in children. Poisoning from common OVER-THE-COUNTER (OTC) DRUGS such as acetaminophen (Tylenol), aspirin, and iron supplements can occur with as few as six or eight tablets, depending on the body weight, age, and health status of the person. Other common sources of poisoning among children are prescription medications that adults, particularly grandparents and older caregivers, are taking. Chronic lead poisoning occurs in children exposed to high levels of lead such as are present in leaded paints applied before 1978.

Falls More than 14,200 people lose their lives in falls each year, nearly two thirds of whom are

age 65 and older. About 7.5 million people require medical attention for accidental injuries received in falls, Falls account for nearly a third of medical visits for accidental injury and are most frequent among those under age 14 (2.3 million) and over age 60 (1.8 million). Child walkers (wheeled chairs prewalking children can push around with their feet) and stairs account for the greatest number of falls among young children. Among older adults, stairs, irregular surfaces, and items such as throw rugs present the most common falling hazards, particularly when lighting is poor as when getting up at night to go to the bathroom. Medication side effects such as drowsiness and balance disturbances often are contributing factors to falls among older adults.

Choking Choking is a significant risk among the very young, the very old, and those who have temporary or long-term SWALLOWING DISORDERS. Choking accounts for 4,200 deaths each year as well as nearly 600,000 medical care visits. Two thirds of choking episodes involve food. Balloons, coins, and candy are also choking hazards for children.

Fires Nearly 4,000 people lose their lives in residential fires each year, most of whom die from inhaling toxic gases and smoke (ASPHYXIATION) rather than BURNS. Health-care providers treat another 500,000 people a year for burns received in residential fires, about half of which are serious enough to result in lifelong disability.

Recreational activities Recreational activities result in 5 million injuries that require medical attention each year. Water activities are the most lethal, accounting for 4,000 deaths annually, with 25 percent of them among children. Basketball, football, and baseball collectively account for the highest number of injuries resulting from participation in structured athletic activities, nearly 1 million per year. Bicycling accidents account for about 500,000 injuries and 800 deaths annually. Each year playground injuries send more than 200,000 children for medical care and over 2 million adults require medical attention for injuries related to overexertion.

Fireworks Though fireworks are illegal in most federal, state, and municipal jurisdictions, fireworks account for more than 9,000 injuries that require medical attention each year. Injuries tend to concentrate in the weeks around the Fourth of July and New Year's Day celebrations. Children are at greatest risk for injuries due to fireworks, two thirds of which are burns. Cuts to the face, fingers, and hands, as well as traumatic AMPUTATION of fingers and vision-threatening EYE injuries, occur most commonly.

Health Consequences of Accidental Injuries

Though many people fully recover from the injuries they receive, some experience residual consequences that may include extended or lifelong disability. Among the most significant of such consequences are

- TRAUMATIC BRAIN INJURY (TBI)
- SPINAL CORD INJURY
- loss of limbs, fingers, and toes
- extensive scarring and disfigurement
- VISION IMPAIRMENT

Even short-term recovery, such as from fractures, burns, and lacerations, disrupts regular activities such as school and work.

Preventive Measures

Many, if not most, accidental injuries are preventable through measures that require little extra effort. Often people are unaware of the risks of their behaviors or believe their participation is not enough to expose them to such risks; for example, driving only a few blocks to the store without wearing a seat belt or turning attention away from a child in a swimming pool to answer the telephone. Overall, however, 90 percent of unintended injuries occur in or within two miles of home.

Key preventive measures among children, for whom accidental injuries carry high risk of serious disability or death, include requiring use of appropriate safety gear and supervision when participating in recreational activities. Health experts estimate that proper helmet use could prevent 80 percent of the 800 deaths and thousands of serious head injuries that result from bicycle accidents, most of which do not involve collisions with motor vehicles, among children and adults alike. Properly worn helmets reduce the risk of

head injury by 80 percent when using skateboards, roller skates, and inline skates as well as for downhill skiing and horseback riding.

Taking small bites and chewing food thoroughly before swallowing are important measures to prevent choking in children and adults. Many older adults use "scheduled DOSE" medication containers that may not be child resistant. A significant portion of poisonings among children occurs when children get into their grandparents' medications. Many medications have coatings that make them taste sweet, giving children the impression that they are candy.

KEY PERSONAL MEASURES FOR PREVENTING ACCIDENTAL INJURIES

- wear seat belts and place children under 60 pounds in appropriate child safety seats in the back seat
- wear a helmet when riding a bicycle or horse, downhill skiing, and wheeled skating, and other appropriate safety gear for sports and athletic activities
- store medications in their original labeled containers, with childproof lids or caps, and in locked cabinets or drawers
- install handrails and lighting for stairways and hallways, and use child gates or child locks to block access to stairs, kitchens, bathrooms, garages, and other hazardous areas
- install handrails in showers and baths, especially for the elderly
- install smoke detectors and put in fresh batteries every six months
- install car horns or buzzers that operate while the vehicle is in reverse

See also ATHLETIC INJURIES; DOMESTIC VIOLENCE; FRACTURE; HEAVY-METAL POISONING; HEIMLICH MANEUVER; HIP FRACTURE IN OLDER ADULTS; NOISE EXPOSURE AND HEARING; OCCUPATIONAL HEALTH AND SAFETY; POISON PREVENTION; VIOLENCE.

antibiotic prophylaxis A DOSE or brief course of ANTIBIOTIC MEDICATIONS before invasive dental, surgical, or diagnostic procedures for people who have had certain HEART operations or who have certain heart conditions to help prevent bacterial ENDOCARDITIS (INFLAMMATION and INFECTION of the heart). Doctors may, though do not always, suggest antibiotic prophylaxis for people who have other heart conditions as well as certain IMMUNE DISORDERS, HIV/AIDS, type 1 DIABETES, active CANCER, and women in LABOR who are group B-strep positive or with prolonged rupture of membranes.

Bacterial endocarditis is a serious infection that can result in permanent damage to the heart, especially the heart valves, or in death. The heart valves are particularly vulnerable to bacteria cultures that establish themselves in their tissues. This risk increases when there are abnormalities of blood flow through the heart that can allow blood to slow or stagnate in the heart's chambers, or when there is damage to the valves that prevents normal movement. Invasive procedures, particularly in the MOUTH (such as tooth extraction or root canal) and gastrointestinal tract, which are rich in natural BACTERIA, provide opportunity for bacteria to enter the bloodstream and travel to the heart.

The typical regimen is a single large dose of an antibiotic one hour before the procedure, usually taken by mouth. The recommended antibiotic is amoxicillin or cephalexin, azithromycin, or clarithromycin for people who are allergic to penicillin. People who are already taking prophylactic antibiotics for other purposes should let their doctors or dentists know; the health-care practitioner will likely choose a different antibiotic for specific prophylaxis to appropriately target the potential classification of bacteria.

ANTIBIOTIC PROPHYLAXIS ADVISED

When Any of These Conditions Exist

cardiopulmonary shunt	cyanotic CONGENITAL HEART DISEASE
HEART TRANSPLANTATION	hypertrophic CARDIOMYOPATHY
mitral valve prolapse with regurgitation	previous bacterial ENDOCARDITIS
RHEUMATIC HEART DISEASE	prosthetic heart valve
	uncorrected congenital heart malformations

Before Any of These Procedures

CARDIAC CATHETERIZATION	CYSTOSCOPY
gastrointestinal ENDOSCOPY	periodontal surgery
placement of bands for braces	prophylactic professional dental cleaning
root canal	surgery (laparoscopic or open)
tissue biopsy	tooth extraction

Though numerous studies suggest the value of antibiotic prophylaxis, none definitively supports or refutes it, giving rise to some disagreement

among health-care providers as to whether it truly lowers the risk for bacterial endocarditis. However, the American Heart Association, the American Dental Association, the Infectious Diseases Society of America, the American Academy of Pediatrics, and the American Society for Gastrointestinal Endoscopy jointly recommend antibiotic prophylaxis in specific circumstances.

See also IMMUNODEFICIENCY; VALVULAR HEART DISEASE.

antismoking efforts The US health community has targeted cigarette smoking since the landmark 1964 surgeon general's report, *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service,* formally identified the connections between smoking and health conditions such as LUNG CANCER, laryngeal CANCER, and chronic BRONCHITIS. A single sentence from the 387-page document summarized what was to become a major preventive health emphasis in the United States for the ensuing decades: "Cigarette smoking is a health hazard of sufficient importance in the United States to warrant appropriate remedial action."

At the time of the 1964 surgeon general's report, 70 million Americans were smokers. The US Centers for Disease Control and Prevention (CDC) reports the number of current smokers remains fairly stable at about 46.2 million, 8.6 million of them becoming ill as a result each year. Health experts project that more than half of people who continue to smoke, about 25 million, will die of smoking-related diseases. Antismoking efforts have a two-prong focus:

1. Encourage people never to start smoking.
2. Encourage people who do smoke to stop, no matter how long they have been smoking.

These efforts emphasize coordinated educational approaches among schools, youth organizations, community organizations, sports and athletic organizations, and health-care providers. As well, a number of class-action lawsuits against TOBACCO companies have forced payments from them to fund health care for smoking-related chronic illnesses and antismoking efforts. General practice guidelines for physicians include screening for tobacco use and recommendation of SMOKING CESSATION methods for people who do smoke.

KEY ANTISMOKING EFFORTS

- intensive education of youth through the schools, advertising, community programs, celebrity advocates, and other targeted approaches
- effective and accessible SMOKING CESSATION methods
- strong warning labels on cigarette packages
- stringent enforcement of age-restricted access to TOBACCO products
- prohibition of smoking in the workplace, public buildings and venues, and other indoor locations

The 1964 report that first linked cigarettes and cancer and subsequent surgeon general's reports on smoking and health are available on the CDC's Web site (www.cdc.gov/tobacco/sgr/index.htm).

See also CANCER PREVENTION; LIFESTYLE AND HEALTH; SMOKING AND CANCER; SMOKING AND CARDIOVASCULAR DISEASE; SMOKING AND HEALTH; TOBACCO USE OTHER THAN SMOKING.

B

birth defects More than 150,000 infants born each year in the United States have structural or functional abnormalities present at birth, ranging from mild to severely debilitating or fatal. Substances and circumstances that can cause birth defects are teratogenic. Some birth defects, notably FETAL ALCOHOL SYNDROME (FAS) and those that occur as a SIDE EFFECT of medications, are entirely preventable. GENE mutations, some of which are hereditary mutations and many of which are spontaneous or isolated mutations, cause many birth defects. The risk for the genetic condition DOWN SYNDROME (trisomy 21), a chromosomal disorder, rises with the mother's age, the only birth defect doctors know for certain does so. Many other birth defects are not preventable, however, and may not be detectable before birth.

The risk for many other birth defects correlates to exposures during PREGNANCY, such as to the viral infections RUBELLA (German measles), CYTOMEGALOVIRUS (CMV), and CHICKENPOX, and to the parasitic INFECTION TOXOPLASMOSIS. These infections can cause mild to significant birth defects, ranging from congenital CATARACT and HEARING LOSS to HEART malformations. Avoiding these exposures prevents any consequential damage to the developing FETUS.

Teratogenic Medications

Doctors widely prescribed the DRUG thalidomide in the 1950s and early 1960s as a treatment for MORNING SICKNESS until they discovered the high incidence of limb deformities associated with its use. Thalidomide marked a turning point in public awareness about the teratogenic hazards of medications as well as in research efforts to identify those hazards. Numerous medications can cause birth defects. The US Food and Drug Administration (FDA), which regulates drug approval and use in the United States, assigns pregnancy categories to medications to help doctors and women assess the risks of using the medications during pregnancy. These categories are

- pregnancy category A: medications for which numerous clinical studies have shown no adverse effects in pregnancy
- pregnancy category B: medications for which animal studies have shown no adverse effects or for which there are limited studies
- pregnancy category C: medications for which there are no studies to indicate either safety or hazard during pregnancy
- pregnancy category D: medications for which clinical studies demonstrate risk to the developing fetus, although the benefits to the mother of the medication may outweigh the risks to the fetus
- pregnancy category X: medications for which clinical studies demonstrate clear evidence of damage to the developing fetus

Doctors generally consider pregnancy category A and B medications safe for women to use during pregnancy, though approach the use of pregnancy category C medications with caution. Women who are pregnant or planning pregnancy should thoroughly discuss benefits and risks with their doctors before taking or continuing to take category D medications and should never take pregnancy category X medications. Pregnant women should check with their doctors or pharmacists about any medications they are taking when they become

COMMON BIRTH DEFECTS

Birth Defect	Health Risk to Infant	Preventive Measures
cleft defects (craniofacial clefts)	negligible with reconstructive surgery difficulty nursing, eating, and with speech when uncorrected	possibly folic acid supplementation GENE mutations have been identified
FETAL ALCOHOL SYNDROME (FAS)	mild to moderate physical deformities, mental retardation, and BEHAVIORAL DISORDERS	abstinence from ALCOHOL during PREGNANCY is fully preventive
genitourinary defects EPISPADIAS HYPOSPADIAS KIDNEY deformities	negligible with reconstructive surgery absence of both kidneys is usually fatal	none known gene mutations have been identified
INFECTION CHICKENPOX CYTOMEGALOVIRUS (CMV) MEASLES RUBELLA TOXOPLASMOSIS HERPES	mild to severe deformities, depending on gestational age at time of infection blindness	vaccination for measles, rubella, and chickenpox prior to pregnancy avoid contact with cat feces (such as through cleaning litter boxes or handling dirt outdoors) and with uncooked meat to prevent toxoplasmosis frequent HAND WASHING to reduce risk for infectious diseases in general
major HEART defects hypoplastic left heart syndrome (HLHS) tetralogy of Fallot transposition of the great arteries (TPA)	significant, with high risk for death lifelong complications remain even with successful surgery these defects are the leading reason for heart transplantation in children	none known comprehensive PRENATAL CARE for early detection and treatment planning; infant will require emergency treatment at birth gene mutations have been identified
minor heart defects ATRIAL SEPTAL DEFECT (ASD) PATENT DUCTUS ARTERIOSUS (PDA) VENTRICULAR SEPTAL DEFECT (VSD)	negligible with appropriate treatment (usually surgical repair)	none known comprehensive prenatal care for early detection and treatment planning gene mutations have been identified
NEURAL TUBE DEFECTS anencephaly SPINA BIFIDA	significant anencephaly is always fatal spina bifida often causes deformity and lower body PARALYSIS, including loss of bowel and BLADDER function	folic acid supplementation before CONCEPTION through the first 28 days of pregnancy cuts risk in half many health experts recommend all women of childbearing age take folic acid supplements (400 micrograms per day) gene mutations have been identified

COMMON TERATOGENIC MEDICATIONS

Medication	Taken to Treat	Kinds of Birth Defects
Pregnancy Category X Medications		
antimetabolitic CHEMOTHERAPY drugs (aminopterin, cytarabine, methotrexate, methyl aminopterin)	CANCER	craniofacial anomalies, anencephaly, absence of kidneys, HEART malformations risk highest in first trimester
danazol (Danocrine)	ENDOMETRIOSIS, FIBROCYSTIC BREAST DISEASE, hereditary ANGIOEDEMA	PSEUDOHERMAPHRADITISM
finasteride (Propecia, Proscar)	male pattern baldness (Propecia), BENIGN PROSTATIC HYPERTROPHY (BPH) (Proscar) *pregnant women are at risk if they handle the pills*	malformation of male GENITALIA
flurazepam (Dalmane)	SLEEP DISORDERS	isolated cleft palate
lovastatin (Mevacor)	HYPERLIPIDEMIA	SPINA BIFIDA
retinoic acid, isotretinoin (Accutane)	severe ACNE	craniofacial anomalies, heart malformations, limb deformities, LIVER malformations highest risk in early first trimester
temazepam (Restoril)	sleep disorders	isolated cleft palate
triazolam (Halcion)	sleep disorders	isolated cleft palate
thalidomide (Thalomid, Synovir)	HANSEN'S DISEASE (leprosy), AIDS-related wasting disease (cachexia)	severely shortened or missing long bones in the arms and legs
warfarin (Coumadin)	blood clots (preventive)	constellation of birth defects commonly referred to as fetal warfarin syndrome multiple skeletal deformities and malformations occur with exposure in early first trimester CENTRAL NERVOUS SYSTEM damage occurs with exposure in second and third trimesters
Pregnancy Category D Medications		
angiotensin-converting enzyme (ACE) inhibitor medications (benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, ramipril, trandolapril)	HYPERTENSION	KIDNEY deformities or absence of kidneys, limb contractures, patent ductus arteriosus (PDA) risk highest in second and third trimesters

Medication	Taken to Treat	Kinds of Birth Defects
angiotensin II receptor antagonist medications (losartan, valsartan, candesartan, irbesartan)	hypertension	heart malformations, kidney deformities or absence of kidneys, widespread organ damage risk highest in third trimester
cimetidine (Tagamet)	GASTROESOPHAGEAL REFLUX DISORDER (GERD), PEPTIC ULCER DISEASE	NEURAL TUBE DEFECTS
phenytoin (Dilantin)	SEIZURE DISORDERS	constellation of birth defects commonly referred to as fetal phenytoin syndrome craniofacial anomalies, deformities of the hands and feet, rib deformities
sulfasalazine (Azulfidine)	INFLAMMATORY BOWEL DISEASE (IBD), especially ulcerative COLITIS	neural tube defects
valproic acid (Depakene)	seizure disorders	craniofacial anomalies, spinal deformities

pregnant and before taking any new medications during pregnancy. The risk for teratogenic effects may increase when a woman takes multiple medications, even when those medications are pregnancy category A and B classifications.

Prenatal Care

PRENATAL CARE lowers the risk for many birth defects. Folic acid (folate) supplementation significantly reduces the risk for NEURAL TUBE DEFECTS such as SPINA BIFIDA and also improves blood GLUCOSE (sugar) control in women who have diabetes. Doctors recommend folic acid supplementation beginning before CONCEPTION when possible, and especially for women who are or have been taking oral contraceptives (birth control pills), which lower folic acid even further. Maternal blood tests for rhesus (Rh) factor and ALPHA FETOPROTEIN (AFP), ULTRASOUND, and in utero diagnostic procedures such as CHORIONIC VILLI SAMPLING (CVS) and AMNIOCENTESIS can detect many birth defects before birth, allowing the mother and her health-care provider to make decisions and appropriate preparations. Other prevention efforts target educating women of childbearing age about the benefits of folic acid supplementation and prenatal care, as well as the risks of behaviors such as alcohol consumption during pregnancy.

KEY MEASURES FOR PREVENTING BIRTH DEFECTS

- folic acid supplementation for all women of childbearing age, whether or not they are pregnant or planning PREGNANCY
- comprehensive PRENATAL CARE during pregnancy
- no alcohol consumption during pregnancy or when attempting to conceive
- vaccination before pregnancy for RUBELLA, CHICKENPOX, MEASLES
- GENETIC COUNSELING when known hereditary conditions exist in either parent or a previous child was born with birth defects

See also ABORTION; CEREBRAL PALSY; CHROMOSOMAL DISORDERS; CLEFT PALATE/CLEFT PALATE AND LIP; CONGENITAL ANOMALY; GENETIC DISORDERS; INHERITANCE PATTERNS.

building-related illness A health condition that arises as the result of problems within a structure, such as an office, school, or home. The US Environmental Protection Agency (EPA) defines a building-related illness (also called a BRI) as one that

- causes clinically observable symptoms and signs, such as COUGH and FEVER, that extend

beyond the length of time a person spends in the building
- doctors can diagnose as a specific condition
- requires correction of an identifiable problem within the building

Building-related illnesses include

- LEGIONNAIRES' DISEASE, a type of PNEUMONIA that results from bacterial contamination of building heating and air-conditioning systems
- upper respiratory illnesses due to toxic molds and fungi
- asbestos-related lung disease
- radon-induced LUNG CANCER
- BRONCHITIS, ASTHMA, chronic LARYNGITIS, pneumonia, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), and cancers resulting from exposure to ENVIRONMENTAL CIGARETTE SMOKE or industrial chemicals

Doctors diagnose and treat building-related illnesses as they would similar illnesses arising from other causes. Because exposure and illness are often chronic, recovery may take extended time. Contemporary building codes and practices help prevent many of the circumstances that cause building-related illnesses, though INDOOR AIR QUALITY remains a significant concern.

See also ASBESTOSIS; ASPERGILLOSIS; LUNGS; RADON EXPOSURE; SICK BUILDING SYNDROME.

C

cancer prevention CANCER claims more than 500,000 lives each year in the United States, and nearly nine million Americans are cancer survivors. Yet all cancers related to TOBACCO use and excessive ALCOHOL consumption are preventable, and cancer experts believe lifestyle changes could prevent a third or more of most other cancers.

The first correlation between a controllable external factor and the development of cancer occurred more than a century ago with the observance that cigarette smokers died younger than nonsmokers. Researchers have since linked cigarette smoking to nearly a dozen types of cancer, notably lung, laryngeal, esophageal, STOMACH, pancreatic, colorectal, prostate, and BREAST cancers as well as myeloid LEUKEMIA. Over the past 40 years scientists have established numerous connections between other external factors and different types of cancer. Many cancer prevention efforts today target those connections, most of which are lifestyle factors. Lifestyle factors associated with an increased risk for many types of cancer include

- tobacco use (particularly cigarette smoking)
- no regular physical exercise
- EATING HABITS that favor high-fat, low-fiber, and low fruit and vegetable consumption
- OBESITY
- excessive alcohol consumption

Though the links between cancer and some lifestyle factors are less than finite, health experts believe lifestyle modifications to minimize the roles of these factors may play in causing cancer could reduce the development of new cancers by about a third and are beneficial for health overall. Some cancers occur as a consequence of chronic INFECTION, such as LIVER CANCER that results from chronic HEPATITIS. Avoiding hepatitis through vaccination and appropriate preventive practices eliminates the cancers it might otherwise cause.

Other cancer prevention efforts target early detection of precancerous and cancerous conditions through screening methods. Early detection allows the highest success for treatment. Nearly all CERVICAL CANCER results from infection with HUMAN PAPILLOMAVIRUS (HPV), which is transmitted sexually, and nearly all COLORECTAL CANCER arises from intestinal polyps. Screenings that detect precancerous conditions, such as intestinal polyps (COLONOSCOPY) and cervical DYSPLASIA (PAP TEST), permit doctors to intervene before the circumstance evolves into one of cancer.

Some health experts advocate taking supplements of antioxidants (such as vitamin C and vitamin E), and in particular COENZYME Q10, to boost the body's ability to resist cancerous growth. Clinical research studies of coenzyme Q10 suggest various health benefits for this potent antioxidant, though to date those investigating the cancer-fighting capabilities of other antioxidants have failed to demonstrate such effect. Consuming substances that decrease inflammatory markers, such as fish oils and aged garlic, may also have preventive benefit.

See also CANCER RISK FACTORS; CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN); LIFESTYLE AND HEALTH; SCREENING FOR CANCER.

cardiovascular disease prevention CARDIOVASCULAR DISEASE (CVD) is the leading cause of death and disability among Americans. It accounts for nearly a million deaths each year and disables as many as 20 million people, limiting their capabilities for work and recreational activities. More than 60 million Americans live with some form of CVD.

SCREENING FOR EARLY DETECTION OF CANCER

Type of Cancer	Routine Screening*
BREAST CANCER	monthly BREAST SELF-EXAMINATION (BSE) annual breast examination from health-care provider annual MAMMOGRAM for women beginning at age 40 years
CERVICAL CANCER	PAP TEST every one to three years beginning with the start of sexual activity or at age 18
colorectal CANCER	annual FECAL OCCULT BLOOD TEST (FOBT) beginning at age 50 in combination with one of the following: • flexible sigmoidoscopy every five years OR • double-contrast BARIUM ENEMA every five years OR • COLONOSCOPY every 10 years
oral cancer (lips and structures of the MOUTH)	annual dental examination
OVARIAN CANCER	annual pelvic examination
PROSTATE CANCER	annual DIGITAL RECTAL EXAMINATION (DRE) to palpate the PROSTATE GLAND for growths beginning at age 45 annual PROSTATE-SPECIFIC ANTIGEN (PSA) blood test beginning at age 50
SKIN CANCER	regular self-examination of all SKIN surfaces skin examination by dermatologist every three to five years after age 40
TESTICULAR CANCER	monthly TESTICULAR SELF-EXAMINATION physician examination with every routine physical for men between the ages of 15 and 35

**For people who have no greater than normal risk for developing cancer. Those who have increased risk because of personal or family health history should follow the recommendations of their physicians.*

Yet health experts believe that nearly 90 percent of acquired CVD is preventable. Though people commonly perceive CVD, also called HEART disease, as a condition affecting older adults, its genesis is often in ADOLESCENCE. Some research studies have found early-stage ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD) in teenagers whose lifestyles are sedentary and feature EATING HABITS high in fast foods.

Age and heredity are primary factors in the development of cardiovascular disease. It is not, at present, possible to do much to change their effects on the cardiovascular system. Doctors consider them fixed (immutable) risk factors that affect every person to some degree. Even in the presence of these risks, however, cardiovascular disease remains primarily the evolution of lifestyle and behavior. These are modifiable (mutable) risk factors; it is possible to change them and thus the influences they exert on the development of cardiovascular disease. Cigarette smoking, OBESITY, lack of regular physical exercise, and eating habits are the leading factors that result in acquired (noncongenital) heart disease. Accordingly, personal prevention efforts target these habits. Key among such efforts are

- SMOKING CESSATION programs

FORMS OF CARDIOVASCULAR DISEASE

ANEURYSM	ANGINA PECTORIS
ARRHYTHMIA	ATHEROSCLEROSIS
BUNDLE BRANCH BLOCK	CARDIOMYOPATHY
cerebral vascular disease (STROKE)	CONGENITAL HEART DISEASE
ENDOCARDITIS	CORONARY ARTERY DISEASE (CAD)
HEART FAILURE	HEART ATTACK
HYPERTENSION	HYPERLIPIDEMIA
ISCHEMIC HEART DISEASE (IHD)	INTERMITTENT CLAUDICATION
MYOCARDITIS	LONG QT SYNDROME (LQTS)
PERICARDITIS	PERIPHERAL VASCULAR DISEASE (PVD)
primary PULMONARY HYPERTENSION	RAYNAUD'S SYNDROME
RHEUMATIC HEART DISEASE	SICK SINUS SYNDROME
VALVULAR HEART DISEASE	WOLFF-PARKINSON-WHITE SYNDROME

- WEIGHT LOSS AND WEIGHT MANAGEMENT programs
- nutrition and dietary education that emphasizes eating habits high in fruits, vegetables, and whole grain products with fewer highly processed and fried foods
- encouraging daily physical exercise through education and activities organized through schools, workplaces, and community organizations
- cholesterol screening with lifestyle modifications and lipid-lowering medications, as appropriate, to maintain healthy levels, and aggressive therapeutic interventions for people who have high blood cholesterol
- BLOOD PRESSURE checks to detect and treat HYPERTENSION
- DIABETES screening programs, as CVD is a leading complication of diabetes and many of the same lifestyle factors contribute to both health problems

Medical interventions can further reduce the effects of lifestyle factors to lower the risk for cardiovascular disease. These interventions may include lipid-lowering medications to reduce CHOLESTEROL BLOOD LEVELS, antihypertensive medications to lower blood pressure, anti-arrhythmia medications to regulate the beating of the heart, and CORONARY ARTERY BYPASS GRAFT (CABG) to replace arteries supplying the heart with blood that are clogged with vascular debris (arterial plaque).

Prevention guidelines established in 2004 take the preventive role of medications a step further, recommending that most people who have heart attacks take a "statin" medication afterward to prevent subsequent heart attacks. Statins belong to the HMG-CoA reductase inhibitor family of drugs that came into widespread use in the 1990s as lipid-lowering medications. Extensive longitudinal studies (studies over time involving varied populations) conducted in several countries, including the United States, demonstrated the further ability of statins to significantly reduce the risk for heart attack in people who have already experienced one or more heart attacks, even when blood cholesterol levels are within heart-healthy ranges.

Because many people do not know they have cardiovascular disease until they have heart attacks or strokes, statin therapy becomes a significant preventive measure for future heart conditions. However, statins deplete COENZYME Q10, an important antioxidant that has powerful anti-inflammatory actions. Taking a coenzyme Q10 supplement while on statin therapy helps restore this vital substance. Many people also benefit from ASPIRIN THERAPY, which provides a mild anticoagulant effect to reduce the risk for blood clots.

LEARN THE WARNING SIGNS OF HEART ATTACK AND HOW TO RESPOND

Health experts recommend that all adults learn the warning signs of HEART ATTACK and become trained in CARDIOPULMONARY RESUSCITATION (CPR). Schools, fire departments, community organizations, and health agencies typically offer CPR classes for minimal or no fee.

Though some studies suggest consumption of red wine lowers the risk for heart disease, most doctors recommend minimizing ALCOHOL consumption overall because of other health risks (such as LIVER disease). Foods that are high in the B vitamins, vitamin C, and vitamin E contain natural antioxidants that help counter the destructive consequences of accumulated metabolic waste (oxidants). Many doctors recommend the nutritional

supplement coenzyme Q10, which several studies have shown can improve the ability of cells to resist damage and to repair themselves. Cardiovascular disease prevention is a comprehensive process that encompasses numerous facets of lifestyle and physiology. The more risk factors an individual can control, the greater the preventive benefit.

KEY MEASURES FOR PREVENTING CARDIOVASCULAR DISEASE

- Do not smoke.
- Get 30 to 45 minutes of exercise daily.
- Eat appropriate portion sizes.
- Eat more fruits, vegetables, and whole grains and fewer processed and fried foods.
- Get regular BLOOD PRESSURE and blood cholesterol level checks.

See also AGING, CARDIOVASCULAR CHANGES THAT OCCUR WITH; ANTIOXIDANT; DIET AND CARDIOVASCULAR HEALTH; LIFESTYLE AND HEALTH; MEDICATIONS TO TREAT CARDIOVASCULAR DISEASE; NUTRITIONAL NEEDS; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH; RISK FACTORS FOR CARDIOVASCULAR DISEASE.

childhood diseases Until the advent of vaccines in the middle of the 20th century, infectious childhood diseases such as DIPHTHERIA and PERTUSSIS (whooping cough) were the leading cause of death among children under age 18. Vaccinations have virtually eliminated some communicable diseases such as SMALLPOX (for which doctors no longer routinely administer vaccinations) and POLIOMYELITIS.

ROUTINE CHILDHOOD VACCINATIONS

CHICKENPOX	DIPHTHERIA
Haemophilus influenzae type b (Hib) pneumonia	hepatitis A
INFLUENZA (the flu)	hepatitis B
MUMPS	MEASLES
pneumococcal pneumonia	PERTUSSIS (whooping cough)
POLIOMYELITIS	RUBELLA (German measles)
tetanus	

Because of vaccination programs, most Americans born after 1970 have not experienced the infectious childhood diseases that caused illness for their parents as children. Some vaccinations are combination products, such as MMR (MEASLES, MUMPS, RUBELLA) and DTP (diphtheria, tetanus, pertussis). Some vaccinations confer lifelong IMMUNITY (protection from INFECTION) while others require periodic booster vaccines.

There is some concern that the mercury in thimerosal, used to preserve some vaccines, exposes young children to levels of mercury that far exceed established guidelines. In 1999 a number of US health agencies joined forces to urge development of thimerosal-free vaccines, which are now available for most vaccines recommended for children age 6 years and younger. Efforts continue to reduce or eliminate thimerosal in all vaccines. Parents should ask for their children to receive thimerosal-free vaccines. When this is not possible, parents should ask for children to receive single-agent rather than combination vaccinations to reduce mercury exposure as much as possible. For nearly all children the benefits of vaccination far outweigh the potential risks associated with mercury exposure.

Children who do acquire the infectious disease rather than receive the vaccination also develop immunity, though the course of the disease can include serious complications and exposes countless other people to infection as well. Measles can cause severe HEARING LOSS, mumps can result in male sterility, and HEPATITIS can cause LIVER failure. Rubella and chickenpox (also called varicella) can cause BIRTH DEFECTS in unborn children whose mothers get the disease in PREGNANCY.

See also HEAVY METAL POISONING; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

community sanitation Some of the most far-reaching improvements in public health have arisen not from laboratory experiments or technological discoveries but rather from the mundane aspects of everyday life. Community health DRINKING WATER STANDARDS, sewage treatment and disposal, and garbage collection and disposal influence health and LIFE EXPECTANCY as much as any medical intervention.

Ancient Rome provides the earliest archaeological evidence of the understanding of these correlations. The city's design featured elaborate networks of aqueducts (water conduits), public toilets and baths, and sewage drainage systems.

These infrastructures established and maintained separation among living areas, clean water, and waste management. Though perhaps implemented as much as for aesthetic purposes as for health reasons, the health benefits of such separations were clear to ancient Romans who wrote about them, such as Marcus Vitruvius Pollio (90–20 B.C.E.) who wrote extensively about Roman architecture and engineering.

Not until the 19th century and its many discoveries in microbiology did physicians finally connect community sanitation, PERSONAL HYGIENE, and public health. In the millennia between, unsanitary and crowded living conditions fostered ravaging epidemics of CHOLERA (from contaminated water); bubonic plague (from flea-infested rats); yellow FEVER (from mosquitoes); and infectious diseases such as TUBERCULOSIS, SMALLPOX, and FOODBORNE ILLNESSES. In such times and circumstances personal bathing was more likely to spread disease than result in cleanliness.

By the start of the 20th century most industrialized countries incorporated public sanitation practices to separate sewage from drinking water supplies and to promote community as well as personal hygiene. Throughout the United States today strict regulations govern community sanitation, establishing processes for disposing of garbage and sewage as well as for maintaining the purity of drinking water and controlling living conditions. However, inadequate sanitation remains a key cause of disease and death in developing parts of the world that lack appropriate mechanisms for community and personal hygiene.

See also HAND WASHING; HEALTH EDUCATION; HEALTH RISK FACTORS; WATERBORNE ILLNESSES.

D

diabetes prevention DIABETES is emerging as one of the most significant health concerns facing the United States in the 21st century. Approximately 18 million Americans have diabetes and 16 million have prediabetes, a condition of INSULIN RESISTANCE that has a high risk for progressing to diabetes. Prevention efforts target type 2 diabetes, which primarily appears in adults as a manifestation of converging lifestyle factors. About 95 percent of diabetes in the United States is type 2, which many researchers and doctors believe appropriate preventive measures that focus on EATING HABITS and physical exercise can eliminate. Type 1 diabetes, which typically features sudden onset in childhood or ADOLESCENCE, is an autoimmune disorder. Most researchers do not consider type 1 diabetes preventable through lifestyle modifications although lifestyle measures can significantly influence insulin EFFICACY and the development of complications related to diabetes.

The discovery of INSULIN replacement therapy in the early 20th century provided the first viable treatment for diabetes, which until that time had been a diagnosis of death. Nearly 100 years later insulin replacement therapy remains the only treatment for type 1 diabetes. In the 1980s oral ANTIDIABETES MEDICATIONS became available to treat type 2 diabetes. Many of these medications work by increasing cellular sensitivity to insulin. Most type 2 diabetes develops over years to decades and manifests after age 40 years, though doctors are diagnosing the condition in an increasing number of adolescents. Doctors and researchers attribute the increase in young-onset type 2 diabetes to the rise in OBESITY among younger people.

Diet and exercise are the major lifestyle factors that contribute to type 2 diabetes. Improvements in both can delay or prevent the disease's development. In particular, exercise improves cell sensitivity to insulin. Numerous clinical studies have shown that 30 minutes a day of moderate physical activity such as walking, coupled with weight loss of 5 to 10 percent, improves insulin resistance more effectively than do antidiabetes medication. Diabetes is a leading cause of CARDIOVASCULAR DISEASE (CVD), KIDNEY disease, blindness, PERIPHERAL VASCULAR DISEASE (PVD), and limb AMPUTATION.

KEY MEASURES FOR PREVENTING DIABETES

- 30 to 45 minutes of physical exercise daily
- weight loss if necessary to achieve a BODY MASS INDEX (BMI) below 25
- diet that features fruits, vegetables, and whole grain products with fewer processed and fried foods
- annual blood GLUCOSE (sugar) test beginning at age 40 years (sooner in women who have had GESTATIONAL DIABETES)

See also AUTOIMMUNE DISORDERS; DIET AND CARDIOVASCULAR HEALTH; PHYSICAL EXERCISE AND CARDIOVASCULAR HEALTH.

drinking water standards Clean water is fundamental to health. In 1974 the US Congress passed into legislation the Safe Drinking Water Act (SDWA), which the Environmental Protection Agency (EPA) administers and enforces. Amended in 1986 and 1996, the SDWA regulates all public drinking water systems in the United States as well as the sources for drinking water supplies. Regulations define the operational parameters for maintaining safe drinking water systems. Though the SDWA does not apply to private wells that serve fewer than 25 people, the US Food and Drug Administration (FDA) encourages those who obtain their drinking water from private wells to maintain similar clean water standards.

HEALTH RISKS OF DRINKING WATER CONTAMINANTS

Contaminant	Potential Health Risks
disinfectants and disinfectant by-products	**localized irritation, CANCER, neurologic, LIVER, KIDNEY**
chlorine, chloramine, chlorite	EYE/NOSE irritation, ANEMIA
bromate, haloacetic acid	increased cancer risk
trihalomethane	increased cancer risk, liver disease, kidney disease, NERVOUS SYSTEM dysfunction
metals and minerals	**neurologic, SKIN, kidney, liver, thyroid, circulatory**
asbestos	INTESTINAL POLYP
arsenic	skin and circulatory problems, increased cancer risk
copper	liver and kidney damage
cyanide	nervous system damage, thyroid dysfunction
lead	developmental delays, kidney damage
mercury	kidney damage
selenium	circulatory damage, HAIR loss
pathogenic microorganisms	**GASTROENTERITIS (NAUSEA, VOMITING, DIARRHEA)**
Giardia lamblia (PARASITE)	GIARDIASIS
Cryptosporidium (parasite)	CRYPTOSPORIDIOSIS
Fecal coliform (BACTERIA)	generalized gastroenteritis
Escherichia coli (bacteria)	*E. coli* gastroenteritis
legionella	LEGIONNAIRES' DISEASE (PNEUMONIA)
organic chemicals	**fertilizers, herbicides, industrial chemical**
altrazine, carbofuran, 1,2-dibromo-3-chloropropane (DBCP), dioxin, ethylene dibromide, methoxychlor	reproductive dysfunction
dichloromethane, dichloropropane, heptachlor, hexachlorobenzene, pentachlorophenol,	increased cancer risk
tetrachloroethylene, trichloroethylene, vinyl chloride	liver dysfunction
alachlor, carbon tetrachloride, chlordane, chlorobenzene, dichloroethylene, endrin, ethylbenzene, lindane	anemia and other blood disorders
benzene, simazine, styrene	immune dysfunction, neurologic disturbances, increased cancer risk, reproductive dysfunction
polychlorinated biphenyls (PCBs)	neurologic disturbances
acrylamide, toluene, xylene	
radionuclides	**increased cancer risk**
radium 226/228, uranium	increase in overall lifetime risk for developing cancer
viruses	**gastroenteritis**
enteroviruses, noroviruses, rotavirus	nausea, vomiting, cramping, diarrhea

Drinking water supplies contain numerous natural and manmade substances that are harmful to health. Under the SDWA, the FDA researches the effects of such contaminants and establishes standards that keep contaminants either out of drinking water supplies or at levels not expected to cause health problems in people with a healthy IMMUNE SYSTEM. These standards may be inadequate to protect people who are IMMUNOCOMPROMISED, such as people who have HIV/AIDS. Local

health departments can provide information about contaminant levels in specific water supplies as well as recommendations for further purifying drinking water. Because it is not always possible to prevent contaminants from entering drinking water sources, water systems typically filter and treat (such as by chlorination) drinking water supplies to reduce contaminants to nonpathogenic levels.

FDA regulations currently address approximately 80 contaminants capable of causing acute (immediate and short term) or chronic (cumulative with exposure over time) health conditions. Among them are

- microorganisms such as BACTERIA (notably fecal coliform and *Escherichia coli*) and parasites
- enteric viruses (viruses that cause gastrointestinal INFECTION)
- disinfectants and disinfectant by-products
- organic and nonorganic chemicals (metals, minerals, and industrial chemicals)
- radionuclides (radioactive particles)

Because scientific knowledge continuously evolves, detecting and eliminating drinking water contaminants is a dynamic process. Generally, state and local water jurisdictions develop the procedures they follow to comply with FDA safe drinking water standards, with input from local health authorities as well as the general public.

See also COMMUNITY SANITATION; ENVIRONMENTAL HAZARD EXPOSURE; FLUORIDATION; WATERBORNE ILLNESSES.

E–F

environmental hazard exposure Numerous substances in the environment create risk for a variety of health problems and conditions. They include pesticides, herbicides, industrial pollutants, minerals and metals, molds and fungi, BACTERIA, viruses, radiation, sewage, garbage, biological waste, and electromagnetic fields. These substances may be naturally occurring or the consequence of human actions, such as manufacturing and agricultural processes. They may cause a wide spectrum of health conditions ranging from hypersensitivity reactions to CANCER.

HEALTH CONDITIONS THAT MAY ARISE FROM ENVIRONMENTAL HAZARD EXPOSURE

- ALLERGIC RHINITIS
- ASTHMA
- brain cancer
- CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)
- FIBROMYALGIA
- HEARING LOSS
- INFECTION
- LUNG CANCER
- METHEMOGLOBINEMIA
- PNEUMONIA
- thyroid disease
- ALZHEIMER DISEASE
- AUTISM
- chronic BRONCHITIS
- DERMATITIS
- EMPHYSEMA
- GASTROENTERITIS
- HEAVY-METAL POISONING
- LIVER CANCER
- MALIGNANT MELANOMA
- MULTIPLE SCLEROSIS
- poisoning

Often, environmental hazards may not directly cause disease but rather become added risk factors that, in aggregate with other factors or circumstances relevant to certain individuals or population groups, increase the likelihood of disease. For example, environmental chemicals may present little risk to the public overall yet confer significant risk on pregnant women. Young children are more likely than adults to experience lead poisoning due to water contamination, not only because of their smaller size but also because their bodies are still developing and cannot yet efficiently clear toxins. People who are IMMUNOCOMPROMISED are highly vulnerable to INFECTION resulting from foodborne or waterborne viruses and bacteria, whereas infection fails to gain a stronghold in people whose immune systems are healthy.

Federal, state, and local agencies oversee administration and enforcement of environmental health laws, regulations, and standards in the United States. Key among them are the US Centers for Disease Control and Prevention (CDC), the National Center for Environmental Health, the US Department of Agriculture (USDA), and the US Environmental Protection Agency (EPA). Collectively, these agencies operate programs to prevent, detect, mitigate, and remedy health conditions arising from exposure to environmental hazards.

See also BUILDING-RELATED ILLNESS; DRINKING WATER STANDARDS; FOODBORNE ILLNESSES; INDOOR AIR QUALITY; RADIATION EXPOSURE; SICK BUILDING SYNDROME; WATERBORNE ILLNESSES.

environmental cigarette smoke People who do not smoke but who live or work among people who smoke in their presence are at risk for the same health conditions that affect smokers, including LUNG CANCER, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), EMPHYSEMA, CARDIOVASCULAR DISEASE (CVD), and chronic BRONCHITIS. Children who regularly breathe cigarette smoke from smokers in the home, also called secondhand smoke or passive smoking, have a much higher rate of chronic OTITIS media (middle EAR INFECTION), ASTHMA, allergies, and chronic bronchitis. Most schools, workplaces, government offices, and

indoor public facilities ban cigarette smoking as a means to reduce exposure to environmental cigarette smoke. Some municipalities in the United States have banned all indoor smoking in locations open to the public.

One measure of cigarette smoke exposure is the blood cotinine level. The body produces cotinine when it breaks down (metabolizes) NICOTINE, the active chemical ingredient of TOBACCO. Researchers believe that while cotinine itself presents no health risk, it provides an accurate measure of exposure to other chemicals, many of which are carcinogenic (cancer-causing), that are present in cigarette smoke. Cotinine is among the chemical federal agencies monitor to assess the health risks of ENVIRONMENTAL HAZARD EXPOSURE.

See also ANTISMOKING EFFORTS; INDOOR AIR QUALITY; LIFESTYLE AND HEALTH; RADON EXPOSURE; SMOKING AND CANCER; SMOKING AND CARDIOVASCULAR DISEASE; SMOKING AND HEALTH.

ergonomics The interactions between people and their physical environments can support or challenge health. The primary role of ergonomics in health is to prevent injuries, particularly musculoskeletal injuries that result from repetitive motions, by identifying interactions that present a risk for injury and implementing interventions to mitigate the risk. Ergonomic interventions may be as simple as rearranging the work area to put commonly used items within easy reach or may require specialized devices and equipment such as telephone headsets, curved handles on tools, nonglare screens for computers, and implements designed specifically for left-handed use.

Ergonomics also evaluates the movements and actions of commonly performed tasks to minimize the risk of overuse to recommend improved methods and techniques. Many job tasks have evolved without formalized attention to the movements they require, with the consequence that employees develop habits for performing the tasks that may not be ergonomically sound. Actions that cause continual reaching across the body, for example, create repetitive stress for the shoulders, back, and neck. Changing the pattern of movement to use the other hand or rearranging the work area to eliminate cross-reaching can signifi-

ERGONOMICS-RELATED HEALTH CONDITIONS

Health Condition	Common Tasks	Remedies
CARPAL TUNNEL SYNDROME	typing, keyboarding, production line, retail scanner	proper technique, ergonomically designed keyboard, frequent movement to stretch fingers and rotate wrists
EYE STRAIN	computer work, watching security monitors, reading, inadequate or inappropriate lighting	eyeglasses to accommodate midrange vision, frequent looking away from task to change focal distance, proper lighting
HEADACHE	noise exposure, bright lights	improved ventilation and airflow
low BACK PAIN	twisting, bending, lifting, extensive walking, prolonged standing	frequent stretching and position changes, proper lift and carry techniques, supportive shoes, shock-absorbent flooring
neck PAIN	holding telephone between chin and shoulder, looking at computer or video monitor, frequently turning head	headset, correct height and distance placement for monitor, rearrange workspace to minimize turning
ROTATOR CUFF IMPINGEMENT SYNDROME	reaching, production line, throwing	reorganize work area to minimize turning, frequent stretching and resting

cantly reduce this stress and its corresponding injuries. An improved method might be as simple as using a footstool or sliding ladder instead of reaching for items on shelves, or could require retraining employees in proper use of equipment and machinery.

Ergonomic factors account for about 4 million injuries among Americans each year, about half of which are serious enough to require medical care or limit participation in daily activities. Ergonomic injuries further account for a third of lost work time. Most of these injuries are musculoskeletal. The US Occupational Health and Safety Agency (OSHA) develops and administers guidelines for ergonomic standards and improvements in the workplace. Though implemented changes to improve the ergonomics of job tasks can prevent future injuries, people who have already experienced ergonomic-related injuries may have long-term or permanent health consequences.

See also ACCIDENTAL INJURIES; OCCUPATIONAL HEALTH AND SAFETY; REPETITIVE MOTION INJURIES.

food safety FOODBORNE ILLNESSES sicken 76 million Americans each year, 5,000 of whom die as a result. Public health efforts target food safety on a community as well as an individual level. At the public safety level, the US Department of Agriculture (USDA) and the US Food and Drug Administration (FDA) oversee numerous programs that regulate food safety in the United States. These programs cover the gamut of food production and include pesticide and herbicide use, animal feed and use of supplements, food additives, product packaging and labeling, and safe food handling practices among wholesalers and retailers (including grocery stores and restaurants). These agencies inspect production facilities and test produce, grains, dairy products, meats, and other foods for biological and chemical contaminants.

The US Centers for Disease Control and Prevention (CDC) monitors foodborne illness outbreaks, in coordination with state and local health departments. These agencies investigate illnesses and recommend corrective procedures to prevent future outbreaks. They also provide education and training for people who work in food services industries. Though the public tends to fear outbreaks of foodborne illnesses that originate from settings such as cruise ships or restaurants, most foodborne illness occurs as a result of contamination in home-prepared foods.

Summertime picnics, holiday parties, and other events where people entertain large groups in their homes or other private venues are common sources of "food poisoning." Nearly always, these events can be traced to improper food preparation, handling, serving, and storage. Using the same surfaces and implements to prepare meat or poultry and then vegetables and fruits allows cross-contamination of BACTERIA that may be present on countertops and cutting boards, in the air, or on foods.

Proper cooking kills the bacteria in the meat or poultry, but raw vegetables and fruits can carry bacteria and the potential for illness to those who eat them. The tendency to leave food out so people may help themselves or while other festivities take place can allow bacteria to flourish. Salads made with mayonnaise, cooked turkey, and pies left out too long at warm temperatures are commonly to blame for foodborne illness. More often than not, contaminated foods look and taste fine.

KEY INDIVIDUAL MEASURES FOR PREVENTING FOODBORNE ILLNESSES

- Wash hands frequently with soap and warm water, especially before and after preparing food.
- Use separate surfaces for preparing meats and other foods.
- Thoroughly cook meats.
- Keep hot foods heated and cold foods chilled when serving them buffet-style.
- Promptly refrigerate leftovers and throw away most leftovers after five days.

See also HAND WASHING; WATERBORNE ILLNESSES.

fluoridation Fluoride is a naturally occurring element that enhances a tooth's ability to retain hardening minerals such as calcium. US federal regulations began requiring communities to add fluoride to their water supplies, when naturally occurring levels of fluoride fall below 0.7 parts per million (ppm), in 1945 as a means of reducing DENTAL CARIES (cavities). Fluoride offers the greatest protection when it is in the bloodstream as the TEETH are forming, so it becomes part of the enamel. Even after the teeth have fully developed,

fluoride continues to interact with the enamel through its presence in the saliva. Dentists also may apply topical fluoride to the surfaces of the teeth for added protection.

The American Dental Association and numerous other health organizations advocate fluoridation, though some groups question the safety of the practice. In the decades since fluoridation became public policy, numerous claims about adverse health effects have surfaced. Investigations of those concerns have failed to produce conclusive evidence to validate them, when fluoride levels are within the established therapeutic ranges. Excessive fluoride consumption can cause dental fluoridosis, in which dark stains appear on the teeth. Though harmless, the tooth stains are permanent. Children should use fluoridated toothpaste in small amounts and with close parental supervision.

See also ORAL HYGIENE.

H

hand washing Frequent hand washing with soap and warm water is one of the most effective means of preventing the spread of infectious diseases. Hand contact is a primary method of transmitting bacterial and viral infections. Hand washing kills or removes most pathogenic agents. To wash the hands:

- Turn on tap to dispense water that is warm but not too hot to hold the hands under its flow.
- Get hands wet.
- Apply soap, preferably liquid soap from a dispenser.
- Work the soap into a lather that covers all surfaces of the hands, taking a full minute.
- Rinse hands under running water.
- If it is not possible to turn off the water without touching the faucet handles, leave the water temporarily running.
- Dry hands thoroughly using disposable towels or a heated air dispenser.
- Use a paper towel to cover the faucet handle, then turn off the water.

WHEN TO WASH THE HANDS

after changing a diaper	after cleaning dirty dishes
after handling raw meat or poultry	after holding an infant
after sneezing or coughing into the hand	after petting or handling animals
after using the bathroom	after sneezing, coughing, or BLOWING THE NOSE
before eating	before holding an infant
before preparing food	before serving food

It is particularly important to wash the hands after going to the bathroom. Fecal-to-oral transmission spreads many gastrointestinal infections. Some studies suggest that many people wash their hands only when they believe someone is observing them. Though hand washing sounds like a simple solution to a complex problem, health experts project it could significantly reduce infectious diseases.

See also BACTERIA; ENTERITIS; FOODBORNE ILLNESSES; GASTROENTERITIS; PERSONAL HYGIENE; TRANSMISSION MODES; VIRUS.

health education Health experts consider instruction about health and disease to be a fundamental dimension of preventive medicine. Health education formalizes such instruction within structured settings such as schools, workshops, and classes. At its most basic level, health education the form of the fundamental instruction children receive in school about the functions of the human body. All states in the United States have governmentally mandated health education requirements, typically for kindergarten (K) through grade 8 or grades K through 12. Other health education curricula may target college-level students. Some health education programs focus on the needs of specific populations, such as childbirth education classes for pregnant women and their partners or DIABETES education classes for people who have diabetes. Businesses may offer health education programs for their employees and their families with the dual goals of improving personal health and reducing time lost to illness or injury.

See also LIFESTYLE AND HEALTH.

health insurance Health insurance is the financial platform for health care in the United States. As such, it plays a significant role in access to

health-care services and in health-care treatment decisions. In 2004, about 250 million Americans had health insurance, just over two thirds through private coverage and the remainder through public programs such as Medicaid and state low-cost health plans.

Nearly all health insurance plans require participants to pay a portion of their medical expenses, typically in the form of annual deductibles and service co-payments. A deductible is payment at the front end, for example, the first $2,500.00 of medical costs each year. A co-payment shares the cost of each health-care service between the person and the insurer, either as a dollar amount or a percentage of the charge. Most plans have a cap on out-of-pocket medical expenses, after which the insurer pays the full amount for covered services. Nonetheless, people who experience serious illnesses or injuries can accumulate significant additional medical expenses for services the insurance plan does not cover. As well, most people pay a portion or all of their health insurance premiums.

Because the US health-care system intricately intertwines health-care services and health insurance, conflicts arise between care needs and insurance coverage. Doctors and hospitals coordinate with insurers to obtain approval for most nonemergency treatments before engaging in them. Most insurers have lists of approved procedures and medications to facilitate the administrative processes and issue payments directly to providers. Each state has laws and rules that regulate how these processes take place and establish procedures for handling disagreements with insurer decisions, and a state insurance commissioner oversees their enforcement.

Though 85 percent of the US population has health insurance and thus access to health-care services, 15 percent does not—about 42 million people. Those who do not have health insurance have great difficulty receiving needed health-care services. The federal government mandates that providers may not deny care to anyone for life-threatening illness or injury and for a pregnant woman's delivery of her child. All states have programs to provide basic health-care services for children and pregnant women. State and local programs attempt to fill in the gaps in providing other care, though the need far exceeds available services.

The intertwining of health insurance and health services that can be an advantage for people who have health insurance becomes a barrier for the 42 million Americans who do not. They frequently go without medical care for conditions that prompt treatment would remedy but that without early intervention become serious and even life-threatening. Preemptive treatment, such as medications to lower blood cholesterol levels or control BLOOD PRESSURE, as well as preventive health measures such as ROUTINE PHYSICAL EXAMINATION, often are out of reach. Many health experts and public health policy planners view the lack of health insurance as one of the most significant challenges facing the health of Americans and the stability of the US health-care system.

See also HEALTH RISK FACTORS; HEALTHY PEOPLE 2010; QUALITY OF LIFE.

health risk factors The variables that create increased vulnerability to illness and injury are numerous and varied. Some health risks are fixed (immutable), such as those related to heredity, gender, and age. Many health risk factors are modifiable (mutable) and correlate to lifestyle and habit. The combination of fixed and modifiable risk factors helps one assess an individual's overall likelihood of developing health conditions such as CARDIOVASCULAR DISEASE (CVD), DIABETES, LIVER disease, KIDNEY disease, COLORECTAL CANCER, LUNG CANCER, PROSTATE CANCER, CERVICAL CANCER, and BREAST CANCER. Though researchers separate fixed and modifiable risk factors from the perspective of health prevention opportunities, within the body the effects of all health risk factors intertwine and affect each other in immeasurable ways.

Fixed (Immutable) Health Risk Factors

Age and gender are the primary fixed risk factors for health. Other fixed health risk factors include personal and family health history (heredity). Though it is not possible to change fixed risk factors, it is possible to influence and somewhat mitigate them through lifestyle and by controlling modifiable risk factors.

Age The risk for many health conditions increases with age as body systems and structures

begin to deteriorate. Age further carries with it the specter of lifestyle choices and their health consequences, often compounding health risk. With increasing age, for example, the body becomes less efficient in its ability to use INSULIN. This increases the risk for type 2 diabetes. Physical inactivity and EATING HABITS may further challenge the body's insulin efficiency, as well as contribute to OBESITY, an independent risk factor for diabetes. In combination, these circumstances significantly boost the likelihood of developing diabetes in older age. Cardiovascular function also becomes less efficient with age, as blood vessels lose elasticity (often as a result of ATHEROSCLEROSIS).

Gender Some health conditions, of course, affect only men (prostate and testicular disorders) or only women (cervical, ovarian, and uterine disorders as well as PREGNANCY-related conditions). Other health conditions may predominantly affect one over the other gender, such as breast cancer. Popular perception erroneously holds that some health problems, such as cardiovascular disease and colorectal cancer, are primarily health risks for men. Though men are more likely than women to develop cardiovascular disease earlier in life, cardiovascular disease is the leading cause of death and disability among men and women alike. Doctors diagnose more women than men with colorectal cancer each year.

Health history PERSONAL HEALTH HISTORY significantly influences future health circumstances and often integrates with lifestyle (modifiable risk factors). Some health conditions are purely of hereditary origin, such as CYSTIC FIBROSIS, HEMOPHILIA, or congenital heart malformations. Some acquired conditions may result in residual health effects, such as chronic OTITIS media (middle ear INFECTION) that may have consequential HEARING LOSS. Other conditions may reflect a genetic predisposition as well as lifestyle choices, such as DIABETES AND CARDIOVASCULAR DISEASE.

Advances in genetics and molecular medicine are making it possible to determine whether a person has a hereditary health condition. Though such knowledge does not change the risk for developing the condition, it does allow the person and his or her doctor to establish a plan for managing the condition. Making changes in lifestyle may delay the condition's development or further mitigate its the adverse effects.

Modifiable (Mutable) Health Risk Factors

Cigarette smoking, eating habits, and physical activity are the primary modifiable risk factors for health. Other health risk factors include occupation, recreational activities, ALCOHOL use, substance abuse, seat belt use, helmet use, and preventive health measures such as vaccination and safer sex practices. Modifiable health risk factors may directly cause disease, such as cigarette smoking, or contribute to the circumstances that allow health conditions to develop, as with diabetes.

Cigarette smoking Since the 1950s, research has linked cigarette smoking with a growing list of health conditions. There are no known health benefits of cigarette smoking. The leading health consequences of smoking are cardiovascular disease and lung cancer. Smoking also causes or contributes to dozens of other health conditions along the entire continuum of life: it influences CONCEPTION, pregnancy, childhood health (ENVIRONMENTAL CIGARETTE SMOKE), nutrition, chronic diseases, numerous cancers, and LIFE EXPECTANCY.

Eating habits The advent of fast food and processed food in the 1960s forever changed eating habits in the United States. Three decades later two thirds of the American population was overweight, a significant general health risk. Most fast foods and processed foods combine low nutritional content and excessive portion sizes.

Fast-food meals often feature "deals" that offer more food for a small increase in price, giving the impression of value. Processed foods, such as quick-prepare meals and snack items, come in packaging often implies the product is a single serving when instead the package contains two, three, or even four servings. When fast foods and processed foods are the mainstay of a person's eating habits, CALORIE consumption often is two to four times what it should be.

Fewer than 20 percent of Americans eat the American Cancer Society's recommended 9 to 12 daily servings of fruits and vegetables, yet more than a third exceed the American Heart Association's guideline limiting dietary fat consumption to 30 percent of total calories. Most Americans need

to eat fewer processed and fried foods and more fruits, vegetables, and whole grain products to meet the nutritional needs of their bodies.

Physical activity Despite the proliferation of gyms, health clubs, and fitness centers over the past few decades, fewer than 20 percent of American adults get the daily physical exercise their bodies need to maintain cardiovascular health and overall metabolic efficiency. Lack of regular physical activity may be more of a factor than eating habits for health maintenance as well as development of health conditions. An adult needs a minimum 30 minutes of sustained, moderately intense, physical activity (such as walking) every day and one to two hours of sustained, moderate to high intensity, exercise (such as swimming, running, bicycling, or basketball) three or four times a week to maintain optimal health.

Obesity Obesity, a combination of factors with eating habits and physical activity at the hub, emerged in the 1990s as an independent health risk factor for numerous health conditions. Key among them are HYPERTENSION (high BLOOD PRESSURE), HEART FAILURE, OBSTRUCTIVE SLEEP APNEA, type 2 diabetes, OSTEOARTHRITIS, infertility, and GALLBLADDER DISEASE. The current clinical standard for assessing health risk associated with body weight is the BODY MASS INDEX (BMI), a mathematical calculation that converts height-and-weight ratio to an aggregate measure of body mass. Researchers have been able to correlate such measures with health conditions and know that lowering BMI, which only occurs through weight loss, correspondingly lowers health risk.

Reducing Personal Health Risk

Health risk factors tend to converge in patterns of increased susceptibility. A person who develops diabetes, for example, acquires an increased risk for cardiovascular disease, kidney disease, and cataracts. As well, the risks for these conditions further increase with age, and family history may also play a role. The key to mitigating health risks is sustained modifications in lifestyle habits that allow a person to maintain optimal health.

Sometimes these modifications are in response to the emergence of health conditions such as cardiovascular disease, diabetes, or cancer. Though the health condition becomes a risk factor as well, changes that improve modifiable risk factors provide cumulative health benefits. For example, a person who has a heart attack may begin walking every day as part of a cardiac rehabilitation program. The regular physical exercise improves cardiovascular health, and over time the person loses 10 or 20 pounds. Blood pressure, blood GLUCOSE (sugar), and blood cholesterol levels also come down.

Nearly everyone can benefit from doing as much as is possible to reduce health risk factors. Seldom is it too late to make changes that improve health and QUALITY OF LIFE.

See also ACCIDENTAL INJURIES; CONGENITAL ANOMALY; DIET AND HEALTH; INHERITANCE PATTERNS; LIFESTYLE AND HEALTH; EXERCISE AND HEALTH; RISK FACTORS FOR CARDIOVASCULAR DISEASE; SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; YOUTH HIGH-RISK BEHAVIOR.

Healthy People 2010 A program of health initiatives that numerous US health agencies jointly sponsor, the goals of which are to improve overall public health in key areas called leading health indicators. The first Healthy People program, Healthy People 2000, evolved from the 1979 US surgeon general's report of the same name. It established criteria for health monitoring and improvement. Various federal and state health organizations structured their objectives and programs to dovetail with Healthy People 2000. Though Healthy People 2000 did not achieve all of its goals, it resulted in measurable improvements in many areas of public health. Healthy People 2010 updates and expands the goals of its predecessor, with annual reports that identify accomplishments and challenges. Healthy People 2010 draws data from existing sources and mechanisms.

Among the participating US federal agencies are the Agency for Healthcare Research and Quality (AHRQ), Centers for Disease Control and Prevention (CDC), US Food and Drug Administration (FDA), Indian Health Service, National Institutes of Health (NIH), Office of Population Affairs, and President's Council on Physical Fitness and Sports. As well, more than 400 state and community

health organizations form the Healthy People Consortium.

HEALTHY PEOPLE 2010 LEADING HEALTH INDICATORS	
access to health care	environmental quality
IMMUNIZATION	injury and VIOLENCE
mental health	overweight and OBESITY
physical activity	responsible sexual behavior
SUBSTANCE ABUSE	TOBACCO use

See also HEALTH RISK FACTORS; LIFESTYLE AND HEALTH.

heavy-metal poisoning Toxicity due to metals such as lead, mercury, copper, and iron can have serious and even lethal health consequences, especially among children. Heavy metals occur naturally in the environment. They are present in soil and in plants that grow underground, and in water. Heavy metals are also the by-products of manufacturing processes. They can quickly accumulate to hazardous levels when they leach into drinking water supplies or enter the food chain when farmers irrigate crops using contaminated water. Some metal pollutants are also present in the air. Numerous environmental laws enacted over the past 30 years have significantly reduced the presence of heavy metals as pollutants; and various standards, such as those for drinking water, require monitoring of metal and mineral levels. The US Environmental Protection Agency (EPA) monitors and enforces these laws.

Lead Federal regulations have banned lead in paints, inks, and gasoline for several decades. Nonetheless lead poisoning continues to be a problem, particularly among children, who are vulnerable to damage at much lower levels of ingestion. Houses built before 1977 may still have leaded paint on the walls and especially wood trim, which young children may peel off and eat. Lead also can enter water supplies when the pipes that carry it are made of lead. As the pipes deteriorate they release lead into the water they carry. Though many larger municipalities have replaced old lead pipes, many smaller ones have not. The smaller body size of children makes them especially vulnerable to toxic accumulations of lead. When the body stops receiving fresh supplies of lead, it can slowly process the lead that has accumulated, and eventually most body systems return to normal.

Mercury The natural forms of mercury are liquid or gas. It forms different chemicals when it combines with other substances. Manufacturing processes combine mercury with oxygen or chlorine to form inorganic combinations, called salts, used in industrial applications such as caustic soda and batteries. Dentists use inorganic mercury compounds in fillings for TEETH. In nature mercury combines with carbon (methylmercury), usually in water, to form organic compounds. These organic mercury compounds accumulate in fish and shellfish.

The liquid nature of mercury has given rise to perceptions that it has mystical or supernatural abilities. Some spiritual and ritualistic practices use mercury, also called quicksilver or azogue, in baths, burned in candles, and sprinkled on surfaces. Like any other form of mercury, however, quicksilver is toxic. Many people who handle, breathe, or ingest quicksilver suffer mercury poisoning.

Excessive amounts of mercury in the body can result in permanent damage to the BRAIN and kidneys. Studies link two forms of mercury—mercury chloride and methylmercury—with an increased risk for developing CANCER. Many people are concerned about the health risks possibly associated with mercury dental fillings (also called dental amalgam). The American Dental Association and the US Food and Drug Administration (FDA), among other health agencies, have issued position statements supporting the continued use of mercury fillings because there are no conclusive studies that correlate its use to mercury poisoning. However, most dentists offer alternative materials for people who are concerned about mercury fillings.

By far the most significant source of mercury among Americans is seafood. In 2004 the FDA issued a health advisory regarding mercury levels in four kinds of fish: swordfish, king mackerel, shark, and tilefish. These fish are at the top of the food chain; they live for many years, subsisting on

a diet of other fish. Methylmercury levels in the flesh of these kinds of fish are higher than in other kinds of fish. The advisory recommends that pregnant women and women who are BREASTFEEDING avoid eating these kinds of fish. Salmon, cod, albacore tuna, pollock, haddock, ocean perch, tilapia, and fresh-water trout have the lowest levels of mercury.

Thimerosal, a common preservative in vaccines and some other biologic agents, contains mercury. Though pharmaceutical manufacturers are moving away from its use, thimerosal remains a concern especially with childhood vaccinations. Individuals should ask for thimerosal-free vaccines and other biologic agents for themselves and for their children. US health agencies have called for the complete eradication of thimerosal as a medicinal preservative.

Copper Though copper occurs in nature, the most common source of human exposure to copper is through water supplies that travel through copper pipes. Water that is highly acidic corrodes the pipes, drawing copper into the water. Excessive copper accumulations in the body can cause irreversible LIVER and KIDNEY damage. Copper also can accumulate in the brain, causing cognitive dysfunction. People who have WILSON'S DISEASE, a hereditary disorder in which the body cannot metabolize copper, are especially vulnerable to copper in the food supply and the environment because copper accumulates in their bodies. The body needs only a very small amount of copper, which it uses to make certain enzymes and to facilitate iron METABOLISM for HEMOGLOBIN production.

Iron The body needs iron to produce hemoglobin, the protein in the blood that binds with oxygen. Iron deficiency is fairly common, and many people take iron supplements. These supplements are the most frequent source for iron poisoning, especially among young children. Excessive amounts of iron in the body slow the HEART RATE and force of contractions, reducing the flow of blood. Other chemical changes that take place at the molecular level affect the ability of cells throughout the body to function. People who have the hereditary condition HEMOCHROMATOSIS cannot properly metabolize iron, resulting in toxic accumulations over years to decades. Iron is also highly toxic to the liver, resulting in hepatonecrosis (death of hepatocytes, the primary functional cells in the liver).

See also DRINKING WATER STANDARDS; POISON PREVENTION.

hepatitis prevention Although acute (sudden and limited) HEPATITIS infections are on the decline in the United States, chronic hepatitis infections (long-term) have reached epidemic proportions. Nearly a third of the US population has had hepatitis A INFECTION, an acute form of the disease that is sudden and limited. While the numbers of new cases are dropping each year because of vaccination and education efforts, hepatitis A remains a significant health threat because it can so easily be transmitted from one person to another. Hepatitis A spreads via oral–fecal contamination as a consequence of failing to wash the hands after using the bathroom. This spreads the VIRUS to items the infected person touches. A significant source of infection is contaminated uncooked foods such as salads. Hepatitis A outbreaks can sweep through schools, day care centers, cruise ships, prisons, and other environments in which large groups of people are in close contact.

Another 7 percent of Americans have chronic forms of hepatitis, either hepatitis B or hepatitis C. The rate of infection for chronic hepatitis is highest among injectable DRUG users and homosexual men (because of bodily fluid contact). Health-care and public safety workers are also at high risk for infection as a result of occupational exposures. However, hepatitis is so pervasive that anyone can become infected without being aware they have been exposed. Some people can carry hepatitis without themselves being sick and usually do not know they are carriers. Yet they can spread the hepatitis virus to others.

Of the five most common hepatitis viruses, fecal–oral contact is the primary infectious route for two: hepatitis A and hepatitis E. These forms of hepatitis are generally acute (sudden and limited). Blood and body fluid contact, such as via sexual intercourse and shared needles among injectable drug users, spread hepatitis B and hepatitis C. Hepatitis D is a risk only for people infected with hepatitis B, as it can replicate only by "hijacking" the hepatitis B virus's genetic material.

Hepatitis C is particularly insidious because the infection can take 20 to 30 years to progress enough to generate symptoms. A blood test can detect antibodies after the virus has been in the body for about six weeks, however, and health experts recommend that people who are at risk for hepatitis C be tested. People at highest risk for having hepatitis C infection are those who may have engaged in high-risk behaviors as long as 20 or 30 years ago. About 4 million Americans have chronic hepatitis C infection, nearly 2 percent of the U.S. population, and epidemiologists believe they may reflect only about 30 to 40 percent of those who are actually infected.

Hepatitis is a significant public health issue. Acute hepatitis sickens thousands of people each year and can be particularly serious, even fatal, in children and in people who are IMMUNOCOMPROMISED. Chronic hepatitis is the leading cause of LIVER FAILURE and leading reason for LIVER TRANSPLANTATION in the United States. A secondary public health concern is that a person who has had hepatitis, or who has chronic hepatitis, cannot donate blood. This has the potential to severely limit the availability of blood and blood products for transfusion.

KEY MEASURES FOR PREVENTING HEPATITIS

- Wash hands frequently with soap and warm water.
- Do not share food, drinks, or eating utensils.
- Receive the hepatitis A and hepatitis B vaccinations.
- Do not use injectable drugs.
- Use condoms during sexual intercourse, and limit sexual partners.
- Use barrier precautions (masks and gloves) to protect against INFECTION from occupational exposure.
- Receive prophylactic treatment (immunoglobulin injection) after suspected exposure.

See also SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION.

HIV/AIDS prevention Researchers first detected the human immunodeficiency VIRUS (HIV) that causes acquired immunodeficiency syndrome (AIDS) in the early 1980s. New HIV/AIDS infections peaked about a decade later and have since slowly but steadily declined to reach a point over the past decade of holding relatively steady in the United States at about 40,000 a year. Advances in treatment, however, have resulted in increasing numbers of people living with HIV. Though this marks an exciting milestone in the fight against HIV/AIDS, it also means the risk for INFECTION is growing because more people are already infected. As well, health experts worry that improved treatment regimens that can forestall the transition from an HIV-positive status to AIDS may encourage complacency about HIV protection. AIDS remains ultimately fatal, and preventing infection remains the only cure. Though medical treatments can delay the disease's progression, there are as yet no treatments that can eradicate the virus. Research continues to search for both a cure and a VACCINE.

Prevention efforts target two dimensions of HIV/AIDS infection, halting the spread of infection and early diagnosis and treatment for those who become infected. Because of the long period of time during which a person can be infected and not know it, health experts view early diagnosis as a preventive measure; because most people, once diagnosed as HIV-positive, will take the recommended precautions to prevent spreading the virus to others. People who do not know they have HIV often do not feel the need to take significant precautions. A special focus area is preventing perinatal infection, in which an HIV-positive woman passes the virus to her unborn child.

Preventing New Infections

A person gets HIV/AIDS from close and regular contact with the body fluids, such as BLOOD and SEMEN, of another person who already has the virus. Abstinence is the only certain way to prevent infection via sexual activity with a partner. Barrier methods to prevent the body fluids of one person from contact with the mucous tissues of the other person during sex are the most effective approaches to reduce the risk for transmitting HIV. Consistent use of latex condoms during sex (anal, vaginal, and oral intercourse) significantly reduces the risk of passing HIV from the infected partner to the noninfected partner. People who inject drugs and share needles and paraphernalia can spread HIV through blood-to-blood contact. Breast milk can also transmit the virus from mother to infant. The average length of time from infection

to symptoms is about 10 years, during which time the person may not know he or she has HIV and can spread the infection to others.

In 1994 HIV/AIDS experts issued a recommendation to test high-risk pregnant women for HIV and to offer those with positive tests treatment with zidovudine (AZT), which slows the rate at which the virus replicates. This allows the infant's IMMUNE SYSTEM to develop sufficiently to produce resistance against HIV and stave off infection. The result was a two thirds reduction in the number of infants born with HIV between 1994 and 1997. Since then, HIV/AIDS programs have made a concerted effort to extend HIV testing and AZT treatment to all pregnant women with the hope that congenital HIV infections will decline even further. Many health-care providers believe HIV testing should be among the routine screenings pregnant women undergo.

Early Diagnosis and Prevention

Nearly a million Americans live with HIV/AIDS yet about 250,000 of them—one in four—do not know they do. The virus can exist in the body for decades without progressing to the disease condition of AIDS. During this time, however, the virus remains active and can spread to other people. By the time symptoms begin to manifest, an important window of therapeutic opportunity has closed. Treatment can still contain the progression of disease for years, but symptoms progress and will increasingly diminish QUALITY OF LIFE.

In 2004 the US Food and Drug Administration (FDA) approved the first rapid test to detect HIV-1 antibodies in a fingerstick blood sample. HIV-1 is the form of the virus that causes nearly all AIDS infections in the United States. More extensive and precise blood tests then confirm positive results. The US Centers for Disease Control and Prevention (CDC) and other health organizations recommend HIV testing become part of the ROUTINE MEDICAL EXAMINATION to facilitate early diagnosis.

KEY MEASURES FOR PREVENTING HIV/AIDS

- sexual abstinence
- when sexually active, latex condom use during every act of sexual intercourse unless in a longstanding monogamous relationship in which both partners have tested negative for HIV
- avoiding injectable drugs
- regular testing for all people who are sexually active
- frequent testing for people who engage in high-risk sexual behaviors (multiple sex partners, unprotected sex) or who use injectable drugs
- early intervention and monitoring for people who are HIV-positive, to start treatment at the most opportune times and to encourage preventive behaviors

See also OCCUPATIONAL HEALTH AND SAFETY; SEXUALLY TRANSMITTED DISEASES (STDS).

I

indoor air quality The average American spends 20 hours or more of each day in various indoor environments such as work, school, and home. Because the air they breathe recirculates, it accumulates pollutants. Indoor air may contain two to five times as much pollution as outdoor air. Health experts believe this contributes to the rise over recent decades in ASTHMA and other respiratory diseases. Indoor air pollutants may be visible, linger as odors, or remain undetected. The risk to health does not necessarily correlate with the ability to detect the pollutant; some of the most hazardous substances (such as carbon monoxide) have no smell or visible presence.

COMMON INDOOR AIR POLLUTANTS

aerosol products	animal dander
asbestos in older structures	BACTERIA
body fragrances	CARBON DIOXIDE
carbon monoxide	cleaning solutions
dust	dust mites
formaldehyde	glues, paints, and solvents
lead	mercury
molds, mildew, and fungi	ozone
particulates	pesticides
radon	TOBACCO smoke
viruses	volatile organic compounds

Ventilation and outdoor air exchange are important for bringing fresh air into the building or home and releasing indoor pollutants so they can disperse. This helps reduce exposure to harmful substances and lower the risk of resulting health conditions. Federal regulations establish ventilation and air exchange rates for commercial buildings. Indoor air also may be too dry or too moist (humid), requiring humidification or dehumidification to make it more comfortable to breathe. Humid air supports the growth of molds and fungi, which can cause hypersensitivity response, ALLERGIC RHINITIS, chronic BRONCHITIS, and other upper respiratory tract conditions. Improperly cleaned humidifiers also can become pathogenic reservoirs, harboring and dispersing colonies of molds and bacteria. Central home heating systems have filters that homeowners or residents must periodically change.

The US Environmental Protection Agency (EPA) administers regulations and standards for indoor air quality, and recommends a three-prong approach:

1. Control pollutants at their sources: This may include no smoking indoors and installing carpets that do not contain VOCs,
2. Ventilate: Open windows and circulating fans move air containing pollutants outside and bring in fresh air.
3. Clean the air: Air cleaners and filters use various methods to extract specific kinds of pollutants from the air. The EPA cautions that air cleaners cannot substitute for proper ventilation and source control as the primary maintenance measures for clean air. Some air cleaners may add different pollutants to the air, such as particulates or ozone.

See also BUILDING-RELATED ILLNESS; ENVIRONMENTAL CIGARETTE SMOKE; LEGIONNAIRES' DISEASE; RADON EXPOSURE; SICK BUILDING SYNDROME.

influenza prevention INFLUENZA, commonly called the flu, is an upper respiratory INFECTION

that causes epidemics (widespread outbreaks of disease) every year. In the United States each year about 20 percent of the population becomes ill with influenza (about 60 million people), and 30,000 to 40,000 people die as a result. Occasionally influenza occurs in a pandemic, in which people worldwide become ill. The most significant influenza pandemic in modern times was the Spanish influenza pandemic of 1918, which sickened 40 percent of the world population and caused more than 20 million deaths. Other pandemics occurred in 1957 (Asian influenza) and 1968 (Hong Kong influenza). Outbreaks of Avian flu created concern among public health officials in the early 2000s but containment efforts prevailed and limited the numbers of people who became ill.

Influenza Virus Strains: Moving Targets

Viruses cause influenza. There are three types of influenza viruses: influenza A, influenza B, and influenza C. Influenza A and B are responsible for most cases of illness; influenza C infections are generally mild and not so easily spread from one person to another as are A and B influenza viruses. Every year the strains of the influenza VIRUS responsible for causing illness are slightly different from the strains that caused infection the previous year (epidemiologists call this "drift"). These changes help the virus survive. Having an influenza infection confers IMMUNITY against the strain of virus that caused it. Because the strains vary each year, however, this immunity has value only for the duration of the flu season in which the virus strain is active (though a small amount of resistance may carry over to similar strains). Epidemiologists and researchers attempt to predict which strains will emerge each year, and base annual influenza vaccines on those strains.

Occasionally the influenza virus makes a dramatic alteration, a phenomenon epidemiologists call "shift." These are the influenza viruses capable of causing pandemic, or worldwide, infection because no immunity exists against them. Health organizations around the world have monitoring systems in place to detect these viruses and respond before pandemic infection develops. Because bird populations serve as reservoirs for influenza viruses that can also infect humans, health officials closely monitor avian influenza infections among birds. Avian influenza outbreaks among domesticated birds in parts of Asia in the late 1990s and early 2000s caused alarm for the potential of a pandemic, though containment responses were effective in confining the outbreaks. The ease with which people travel around the world creates considerable challenge for containing outbreaks.

Influenza Vaccination

Vaccines provide immunity by stimulating the IMMUNE SYSTEM enough to produce antibodies to fight the virus at its next attempt to enter the body but not enough to cause illness. The resulting immunity is effective against only the specific strain of virus. Two kinds of influenza vaccines are available in the United States:

- The conventional flu shot contains inactivated (killed) influenza virus, which, when injected into the body, cause the immune system to respond. The first killed-virus influenza VACCINE became available in the United States in 1945. Anyone older than six months of age can receive the flu shot.
- The live attenuated vaccine, which comes in the form of a nasal spray, contains live but weakened influenza virus genetically altered so it cannot cause illness (it is unable to survive at body temperature). The weakened virus enters the bloodstream via the mucous membranes of the nasal passages. Like the inactivated influenza injected vaccine, the live attenuated vaccine activates an immune system response to produce antibodies. The live attenuated influenza vaccine became available in the United States in 2003. Only people between the ages of 5 and 49 who are healthy can receive the live attenuated virus.

Health experts recommend getting the influenza vaccine in October or November, as the flu season in the United States typically runs December to March each year. Though everyone can benefit from vaccination, certain groups of people are at high risk for infection. They include

- children between the ages of six months and 2 years as well as their household members
- people age 50 and older
- people who live in extended-care facilities and other group settings
- people who work in health-care and public safety positions
- people over age six months who have chronic health conditions

Occasionally there are shortages of vaccine, as occurred in 2004, which is a significant public health issue. When this occurs, public health agencies such as the US Centers for Disease Control and Prevention (CDC) and the US Department of Health and Human Services (HHS) issue revised guidelines to protect those who are most vulnerable to complications.

Antiviral Medications

Because influenza is a viral infection, most treatment measures are supportive and target symptoms. From a prevention standpoint, ANTIVIRAL MEDICATIONS that can reduce the severity of symptoms can also reduce the spread of influenza infection. A doctor must prescribe an antiviral medication within 48 hours of the onset of symptoms; the more quickly after exposure, the more effective the medication. Antiviral medications available in the United States include amantadine (Symmetrel), rimantadine (Flumadine), zanamivir (Relenza), and oseltamivir (Tamiflu).

Frequent HAND WASHING and sneezing or coughing into a tissue or the sleeve rather than the hands are among the most effective measures for preventing the spread of the influenza virus from person to person.

See also INCUBATION PERIOD; TRANSMISSION MODES.

L

life expectancy A statistical calculation representing how many years a person might expect to live. Simple life expectancy calculates projected years of life from birth. Age-adjusted life expectancy projects how many more years a person of a certain age might expect to live. It is important to remember that such calculations are projections, not factual assertions of how long an individual will live. Any individual may live longer or less than his or her life expectancy as a result of numerous variables.

Life expectancy at birth has steadily increased in the United States, climbing by 60 percent overall between 1900 and 2000. A child born in 1900 could expect to live about 48 years, whereas a child born in 2000 could expect to live about 77 years. Though life expectancy for men remains less than that for women, the gap is slowly closing. Some health experts believe discoveries in genetics and molecular medicine in the early years of the 21st century have the potential to extend life expectancy 15 to 25 percent within the next decade.

Increases in life expectancy have historically reflected improvements in numerous areas of public health, ranging from sanitation to vaccinations. Current increases reflect health and healthcare improvements primarily in areas such as pharmaceuticals, diagnostic procedures that allow early detection of potentially fatal health conditions, and therapeutic technologies. Individual variables such as family and PERSONAL HEALTH HISTORY also influence life expectancy, as do behaviors that affect health such as cigarette smoking. Numerous government agencies publish life expectancy data, updated annually.

See also HEALTH RISK FACTORS; LIFESTYLE AND HEALTH; IMMUNIZATION; YOUTH HIGH-RISK BEHAVIORS.

lifestyle and health Many aspects of lifestyle influence health. Among the most significant are

- cigarette smoking and other tobacco use
- diet and nutrition
- physical activity and exercise
- occupational health risks
- WEIGHT LOSS AND WEIGHT MANAGEMENT and OBESITY
- seat belt and helmet use
- SAFER SEX PRACTICES

The correlations between lifestyle behaviors and health conditions are both direct and indirect and often intertwined. Numerous research studies show conclusively, for example, that cigarette smoking is a direct cause of CARDIOVASCULAR DISEASE (CVD), LUNG CANCER, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), laryngeal CANCER, and STOMACH CANCER and a contributing cause to numerous other cancers and diseases. Scientists and researchers know, too, that OBESITY is a clear factor in health conditions such as cardiovascular disease and DIABETES. Furthermore, diabetes is one of the leading causes (along with cigarette smoking and obesity) of cardiovascular diseases such as HYPERTENSION (high BLOOD PRESSURE), PERIPHERAL VASCULAR DISEASE (PVD), and CORONARY ARTERY DISEASE (CAD).

Researchers also know that diet and nutrition are key factors in healthy body function as well as in disease states. Some diseases result directly from nutritional deficiencies, such as pernicious ANEMIA (vitamin B_{12} deficiency, which can occur from dietary insufficiency or due to MALABSORPTION disorders, PEPTIC ULCER DISEASE, or GASTRECTOMY). Researchers continue to investigate the ways in which nutritional and dietary factors contribute indirectly to health conditions, particularly with

respect to the disease-fighting potential of antioxidants. Cancer researchers have made connections between the body's ability to fight off cancer and dietary habits such as eating 9 to 12 servings a day of fruits and vegetables.

Health conditions may also affect EATING HABITS, with further consequence for health and well-being. People who have LACTOSE INTOLERANCE, for example, cannot consume dairy products, the most common source of calcium and vitamin D. It is important for them to obtain these nutrients through other foods and through supplements. Some medications may require dietary restrictions. For example, people who take monoamine oxidase inhibitor (MAOI) medications, prescribed to treat DEPRESSION and occasionally to treat PARKINSON'S DISEASE, cannot eat foods such as cheeses and smoked meats that contain the amino acid tyramine. Health conditions may also limit what a person can eat; for example, a person who has CELIAC DISEASE (sprue) cannot eat foods that contain gluten.

Physical inactivity has come under intense scrutiny from health experts in recent years as more evidence emerges to connect physical activity with health and sedentary habits with disease. Though scientists do not fully understand the myriad ways in which exercise affects cell activity, they know that it increases INSULIN sensitivity and results in overall improved metabolic efficiency. In a sense, regular physical activity seems for the body like a tune-up is for a car—it keeps it running as smoothly as possible. Health experts urge people to get a minimum of 30 minutes of physical exercise, such as walking, every day.

The correlations between lifestyle and health take on particular relevance in the context of the aging of the American population. As people are living longer, QUALITY OF LIFE becomes an increasingly significant focus. Advances in medical technology now allow routine treatments for conditions that only a few decades ago were deadly. Thrombolytic medications can halt and even reverse HEART ATTACK and STROKE due to blood clots. ORGAN TRANSPLANTATION extends the promise of normal life to thousands of Americans. Prosthetic joints restore movement when arthritis or injury destroys joints and bones. Yet within the framework of these advances remains the reality that individual health is an individual responsibility. Medical science can fix quite a lot but the way in which a person chooses to protect the functions and structures of his or her body plays a significant role in health.

See also COENZYME Q10; OBESITY, HEALTH CONSEQUENCES OF; OCCUPATIONAL HEALTH AND SAFETY; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SMOKING AND HEALTH.

N–P

neural tube defects BIRTH DEFECTS in which the neural tube, the precursor to the SPINAL CORD and BRAIN, fails to develop properly. The neural tube develops in the first few weeks of gestational life and may be complete by the time a woman knows she is pregnant. An open neural tube defect exposes the brain and spinal cord outside the body. SKIN and spinal structure abnormally encase a closed neural tube defect, typically involving only the spine (and usually the lower spine). Though there are associations between neural tube defects and CHROMOSOMAL DISORDERS such as DOWN SYNDROME, most researchers believe neural tube defects occur as a combination of random GENE MUTATION and environmental circumstances.

The most serious neural tube defect is anencephaly, in which the brain does not form. Anencephaly is always fatal. SPINA BIFIDA, in which the spinal column does not close properly, can result in mild to debilitating deformity and disability. The mildest form of spina bifida is myelomeningocele, in which the defect affects only a small portion of the lower spinal cord. Reconstructive surgery can improve protection of the spinal cord, though a degree of PARALYSIS affecting bowel, BLADDER, and lower body function typically remains. Occasionally a neural tube defect is so minor that it does not become apparent until later in life, even adulthood.

Folic acid supplementation, ideally beginning before CONCEPTION, can prevent most neural tube defects. Health experts recommend all sexually active women of childbearing age take folic acid supplements whether or not they plan PREGNANCY. (Folic acid supplementation also helps stabilize blood glucose levels in pregnant women who have DIABETES.) ALPHA FETOPROTEIN (AFP), CHORIONIC VILLI SAMPLING (CVS), and prenatal ULTRASOUND can detect most neural tube defects before birth, allowing women and their doctors to make decisions about the course of the pregnancy and care needs following birth. Doctors often recommend terminating the pregnancy when the neural tube defect is so severe that death of the infant would be certain and immediate after birth.

See also ABORTION; CONGENITAL ANOMALY; KYPHOSIS; SCOLIOSIS.

occupational health and safety Work-related injuries account for about 6,000 deaths and 16 million health-care visits each year in the United States. There are literally thousands of hazards in the workplace, some common to nearly all jobs and others unique to specific occupations. In the United States, the Department of Labor, the Occupational and Health Safety Agency (OSHA), the Centers for Disease Control and Prevention (CDC), and the National Institute for Occupational Safety and Health (NIOSH) oversee workplace safety regulations, standards, and procedures. OSHA further has enforcement authority for compliance issues. Other federal and state organizations also participate in workplace safety.

MOST COMMON CAUSES OF WORKPLACE FATALITIES IN THE UNITED STATES

drowning	ELECTROCUTION
falls from roofs and ladders	fires and explosions
MOTOR VEHICLE ACCIDENTS	overturned equipment
struck by falling objects	substance exposure
suicide	VIOLENCE

Employers are responsible for providing a working environment free from unreasonable risk to workers. Such an environment varies according to occupation. To the extent possible, federal and

state laws mandate appropriate protective measures for workers in high-risk occupations. Occupational and industry standards often result in further measures to protect people from the hazards of their jobs. Individuals are responsible for following appropriate safety procedures.

MOTOR VEHICLE ACCIDENTS account for about 25 percent of workplace deaths. VIOLENCE also claims a significant number of deaths, particularly among retail cashiers and cab drivers who are at risk for death by homicide during robberies. Other occupations with high risk for injury and death are logging, commercial fishing, roofing, construction, and mining.

KEY INDIVIDUAL MEASURES FOR PREVENTING WORKPLACE INJURIES

- Obtain proper training for operating devices and equipment.
- Integrate ergonomic standards and practices into work stations and job tasks.
- Use appropriate protective devices, clothing, and gear.
- Follow employer risk-management policies and procedures.
- Remain DRUG-free and ALCOHOL-free in the workplace.

See also ACCIDENTAL INJURIES; BUILDING-RELATED ILLNESS; OCCUPATIONAL HEALTH AND SAFETY; REPETITIVE MOTION INJURIES; SICK BUILDING SYNDROME; TRAUMA PREVENTION; WORKPLACE STRESS.

personal health history An ongoing record of an individual's health conditions including vaccinations, illnesses, injuries, operations, pregnancies and births, medications, and other information that might be relevant in the context of providing health-care services. A personal health history also helps determine future health risks and appropriate treatment options.

A personal health history might include these events (including dates)

- vaccinations, routine medical examinations, and routine diagnostic procedures such as MAMMOGRAM, PAP TEST, blood cholesterol test, tuberculin SKIN test, COLONOSCOPY
- common childhood diseases such as MEASLES, MUMPS, RUBELLA, CHICKENPOX
- uncommon childhood diseases such as SCARLET FEVER, rheumatic FEVER
- congenital anomalies, BIRTH DEFECTS, and congenital disorders (such as CEREBRAL PALSY), or GENETIC DISORDERS (such as SICKLE CELL ANEMIA or HEMOPHILIA)
- serious injuries such as BONE FRACTURE, CONCUSSION, major trauma
- serious illnesses such as ENCEPHALITIS, MENINGITIS, ENDOCARDITIS, HEPATITIS, PANCREATITIS
- surgeries (including TUBAL LIGATION or VASECTOMY)
- pregnancies, miscarriages, abortions, deliveries
- CONTRACEPTION, SEXUALLY TRANSMITTED DISEASES (STDS)
- DIABETES
- CARDIOVASCULAR DISEASE (CVD)
    - HEART ATTACK or STROKE
    - HYPERTENSION (high BLOOD PRESSURE)
    - ANGINA PECTORIS
    - ARRHYTHMIA
    - PERIPHERAL VASCULAR DISEASE (PVD), CORONARY ARTERY DISEASE (CAD), or CORONARY ARTERY BYPASS GRAFT (CABG)
    - HEART FAILURE or CARDIOMYOPATHY
    - VALVULAR HEART DISEASE or valve replacement
- pulmonary disease such as CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) or EMPHYSEMA
- gastrointestinal disorders such as INFLAMMATORY BOWEL DISEASE (IBD), GASTROESOPHAGEAL REFLUX DISORDER (GERD), PEPTIC ULCER DISEASE
- CANCER (including SKIN CANCER)
- neurologic conditions such as PARKINSON'S DISEASE or psychiatric conditions such as SCHIZOPHRENIA or BIPOLAR DISORDER
- chronic health conditions
    - infections such as OTITIS media, SINUSITIS, BRONCHITIS, CYSTITIS
    - OSTEOARTHRITIS, ANKYLOSING SPONDYLITIS, GOUT
    - thyroid disease such as HYPOTHYROIDISM, GOITER, or HYPERTHYROIDISM
    - DEPRESSION or GENERALIZED ANXIETY DISORDER (GAD)
- medications (including OVER-THE-COUNTER [OTC] DRUGS and herbal remedies)

- lifestyle factors such as smoking, EATING HABITS, physical exercise, and occupational health risks

It also is helpful to know about the general health histories of immediate family members (parents, siblings, and children), particularly in regard to health conditions that can have familial tendencies such as diabetes, cancer, and cardiovascular disease.

See also HEALTH RISK FACTORS.

personal hygiene Until researchers discovered BACTERIA and connected them with INFECTION, doctors went from one patient to another without washing their hands, and people did not bathe or otherwise manage personal hygiene. Before the 20th century most people believed bathing caused rather than prevented illness. Because sewage and garbage often contaminated water supplies, this all too frequently turned out the case. Doctors now know that cleanliness prevents the spread of many kinds of infection and disease. COMMUNITY SANITATION measures provide strict procedures for managing wastes, and clean DRINKING WATER STANDARDS help maintain the purity of water that flows from the tap.

Personal hygiene—regular bathing and cleansing of the body—helps control body odor, the result of bacterial growth on the SKIN (especially the underarms) in interaction with perspiration the body releases. It also can help prevent conditions such as athlete's foot and jock itch (types of yeast infections) and reduce the risk for bacterial infection following skin wounds such as cuts and scrapes.

See also HAND WASHING; HYPERHIDROSIS; NOSOCOMIAL INFECTIONS.

poison prevention Poisoning is the third-leading cause of ACCIDENTAL INJURIES, often affecting children who ingest toxic plants, cleaning products, and medications (over-the-counter as well as prescription). Poisoning also may affect adults when they consume more of a medication than is safe or plants and other substances that are toxic.

National poison control hotline:
1-800-222-1222
Available 24 hours a day, 7 days a week, from anywhere in the United States

Children especially are attracted to medications that are brightly colored and that may have a sweetened coating intended to make them more palatable to swallow. Medications designed for children are sweetened, chewable, or in other ways made enticing. Careful storage of potentially poisonous products could prevent many accidental poisonings. Older adults who are not accustomed to having children around or who have difficulty managing child-resistant closures often keep their medications in other containers or dispensers. This practice is a tragically frequent source of poisoning in children who find the containers and think they hold candy.

COMMON POISONOUS YARD AND HOUSE PLANTS

acorns	azalea
buckeyes	buttercups
castor bean seeds	crocus bulbs
daffodil bulbs	daphne berries
deadly nightshade	dieffenbachia
elderberry	foxglove
hyacinth bulbs	jack in the pulpit
jasmine berries	larkspur seeds
lily of the valley	mayapple
mistletoe berries	moonseed berries
mushrooms and toadstools	narcissus bulbs
oleander leaves and branches	poison hemlock
red sage berries	rhododendron
rhubarb leaves	thorn apple
wisteria	yew

Many decorative indoor and outdoor plants are poisonous, presenting a hazard especially for children young enough to put everything in their mouths and older children who may use leaves, berries, and branches as "play" food. Some common plants, such as oleander, are so toxic that plant juice on the hands can cause serious and sometimes fatal illness. Adults should teach children to never pick and eat any kinds of berries, fruit, leaves, mushrooms, nuts, or even sticks to use for campfire cooking without a knowledgeable adult's supervision and approval.

Do *not* give anything to, or induce vomiting in, a person who may have consumed a toxic substance, unless the substance is known and its original package or product label contains specific instructions for poisoning. Otherwise, contact

emergency medical assistance (911, a hospital emergency room, or the national poison control hotline at 1-800-222-1222) and follow the recommended actions.

KEY MEASURES FOR PREVENTING POISONING

- Store all medications in their original labeled containers, with child-resistant lids or caps, in a locked cabinet or drawer out of the reach of children.
- Accurately measure medication doses, especially those given to children.
- Clear yards and play areas of toxic plants.
- Store cleaning products in locked cabinets out of the reach of children.

See also CONTACT TOXINS; INGESTED TOXINS; INHALED TOXINS; INJECTED TOXINS; OVERDOSE.

preventive health care and immunization Prevention measures are the mainstay of preventive medicine. Many such measures relate to lifestyle, such as smoking, EATING HABITS, and physical exercise. Others involve vaccinations to prevent disease and ROUTINE MEDICAL EXAMINATION and screening procedures to detect health conditions for early intervention and treatment. Key self-care measures are BREAST SELF-EXAMINATION (BSE) for women and for men, TESTICULAR SELF-EXAMINATION (TSE) for men, and SKIN self-examination for men and women. Immunizations provide protection against numerous potentially serious or life-threatening illnesses.

Recommendations for doctor examinations and screening tests vary according to gender and age. Appendix X, "Immunization and Routine Examination Scheldules," provides comprehensive information for infants and children, adolescents, men, and women.

See also HEALTH RISK FACTORS; LIFESTYLE AND HEALTH; TRAVEL IMMUNIZATIONS; VACCINE.

Q–R

quality of life The extent to which health supports, and disease or injury prevents, a person's ability to participate in and enjoy daily living activities is highly subjective though nonetheless a crucial measure of health care. Health experts use various tools, such as questionnaires, and methodologies to assess health-related quality of life (HRQOL). The findings become integral in determining the overall effectiveness of intervention and treatment approaches for all kinds of health circumstances from surgical operations to degenerative diseases.

Numerous factors influence quality of life for people living with chronic health conditions or disabilities, ranging from personal satisfaction with the process and outcome of medical treatment to the removal of barriers to participation in activities of interest. Removing barriers might include measures such as adaptive devices for HEARING LOSS and VISION IMPAIRMENT, voice-activated telephones and other electronics, prosthetic limbs, and mobility devices. Each person has activities that he or she considers essential for enjoying life.

Individual satisfaction with of quality of life correlates closely to expectations for outcomes, which vary among cultures and generations. Younger people tend to have higher expectations for treatments that return them to "normal" in relatively short order. Medical technology often makes such expectations reality. However, technology has its limitations and sometimes expectations exceed them. Doctors may be excited about the potential of new treatments, and individuals may be less than fully informed about potential benefits and risks. Taking the time to thoroughly investigate proposed treatments, including medications and surgeries, and obtaining second opinions from other doctors are key measures that can help put those treatments in proper perspective and frame realistic expectations.

Quality of life is a particular concern for people who have severely debilitating or terminal health conditions. Issues such as independence, mobility, PAIN management, and dignity often arise. Most people are more accepting of chronic and even terminal conditions when they are able to discuss their concerns and fears openly and honestly with their doctors, and to establish treatment plans that are consistent with their wishes.

See also ADVANCE DIRECTIVES; CULTURAL AND ETHNIC HEALTH-CARE PERSPECTIVES; END OF LIFE CONCERNS.

radon exposure Radon is a naturally occurring radioactive element, present as a gas in rocks and soil. Radon is also a CARCINOGEN (cancer-causing substance) that is the second-leading cause of LUNG CANCER in the United States. The highest rate of radon-induced LUNG cancer occurs among miners who work underground and breathe concentrated levels of radon over years to decades. Cigarette smoking, in addition to itself being the leading cause of lung cancer, greatly increases the risk for radon-induced lung cancer. Radon becomes a general health hazard when its levels rise inside houses and workplaces such as offices and stores. It seeps inside through cracks in foundations and floors, often drawn indoors by pressure inequalities (the air inside is generally lower pressure than the air outside).

The US Environmental Protection Agency (EPA) has established an "action level" for indoor radon concentrations of 4 picocuries per liter (pCi/L). The typical house has a radon concentration of about 25 percent of the maximum, 1.0 to 1.25 pCi/L; the air in an underground mine may contain four times the maximum, 20 pCi/L, or

even more. Outdoor air typically contains about 0.4 pCi/L of radon. There is no determined safe level of radon. The public health goal is to lower all indoor radon levels to 2 pCi/L or less, with the eventual goal of lowering indoor radon levels to those of outdoor radon levels.

Home test kits, available through state radon offices and radon mitigation contractors, can measure radon levels. Among the most common methods for lowering indoor radon levels are beneath-ground ventilation systems that collect radon from under a house and release it via ventilation tubing into the outdoor air. These systems often can accommodate any kind of foundation (basement, slab, or slab with crawl space). Health experts recommend initial radon testing with regular follow-up testing regardless of the level.

See also ENVIRONMENTAL HAZARD EXPOSURE; HEALTH RISK FACTORS.

routine medical examination The examination a doctor conducts to assess an individual's health status typically includes certain procedures and tests that vary according to age and gender. A routine medical examination for adults consists of a physical examination, PERSONAL HEALTH HISTORY, general BLOOD tests (complete blood count [CBC], blood GLUCOSE, blood cholesterol), and URINALYSIS. Depending on the person's age, the doctor may order other diagnostic procedures such as blood tests for thyroid hormones, chest X-RAY, tuberculin skin test, COLONOSCOPY, MAMMOGRAPHY, and BONE DENSITY testing.

Some of the devices the doctor may use to assess physical health include

- ophthalmoscope to visualize the structures of the EYE
- otoscope to look at the structures of the outer EAR and the eardrum (TYMPANIC MEMBRANE)
- STETHOSCOPE to listen to the HEART and LUNGS (AUSCULTATION)
- sphygmomanometer to measure the BLOOD PRESSURE
- thermometer to take the temperature
- REFLEX hammer to test reflexes and other neurologic responses
- tuning fork to screen hearing and to assess sensory perception (neurologic function) in other parts of the body

Each doctor has his or her pattern for conducting a physical examination. A common pattern is to begin with vital signs and then go from head to foot.

Vital signs The typical vital signs are PULSE, RESPIRATION RATE, temperature, blood pressure, height, and weight. Temperature identifies whether there is a FEVER. Height and weight help the doctor to assess BODY MASS INDEX (BMI) and the likelihood of certain health conditions that correlate to body weight. Many doctors will take blood pressure readings at the start and end of the examination, because a person's anxiety about the examination may cause blood pressure to be artificially elevated. The doctor will typically take the pulse at each wrist and ankle, pressing against the pulse point with two fingers, and may check the pulses in the neck and groin as well. Respiration rate includes a count of how many breaths the person takes in a minute as well as an assessment of how deep or shallow the breaths are.

Head, face, and neck The doctor looks in the ears and the eyes, and may hold a tuning fork near each ear as a basic hearing screen. Many doctors use a SNELLEN CHART to assess basic visual acuity. When the doctor says, "Say ah," the sound causes the soft palate and related tissues at the back of the MOUTH to elevate. This allows the doctor to visualize the top of the THROAT. Sometimes the doctor presses a tongue depressor against the back of the mouth for a better view, which can unintentionally activate the GAG REFLEX. The doctor also looks at the structures of the mouth including the tongue. Palpating the neck helps identify thyroid nodules and enlargement; the doctor usually will feel the neck twice, first with the person sitting quietly and then when having the person swallow.

Chest The doctor listens to the heart and lungs with a stethoscope, and may tap on the chest and the back. The stethoscope allows the doctor to hear the heart valves open and close and the rhythm of the heart as it beats. It also lets the doctor hear the sounds of air entering and leaving the

lungs (breath sounds). The tapping helps to identify areas of unusual density that might suggest enlargement of the heart, accumulated fluids, or other circumstances that need further examination. The chest examination should also include breast examination for men as well as women, to detect lumps or other abnormalities.

Back The doctor may look at the back from the back and each side when the person is standing, as a general screen for SCOLIOSIS, KYPHOSIS, and other back conditions. The doctor may palpate the spine and have the person raise and lower the arms to examine the shoulders and shoulder blades. The back also is a common site for ACNE, ACTINIC KERATOSIS, and other SKIN conditions.

Abdomen The doctor palpates the abdomen from the base of the ribs to the pelvis, feeling for any usual masses or tenderness. Abdominal palpation helps detect signs of ASCITES (collected fluid in the abdominal cavity) abdominal ANEURYSM (weakening and ballooning of the major ARTERY in the abdomen, the AORTA), LIVER or SPLEEN enlargement, and tenderness of organs such as the GALLBLADDER, STOMACH, and pancreas. The doctor will also listen to the abdomen with a stethoscope, further checking for abdominal aneurysm as well as assessing BOWEL SOUNDS. The doctor may also tap on the belly, listening for differences in tones that might suggest changes in density.

Arms and legs The doctor may move the arms and legs to examine the joints, MUSCLE tone, and range of motion. Small taps with the reflex hammer test TENDON responses as well as neurologic reflexes. The doctor looks for unusual bruising, swelling or edema, discolorations, and disparities between sides of the body. The doctor may observe as the person walks across the room and back to assess gait and balance. Pulses in the feet are good indicators of peripheral circulation.

Genitalia The doctor will palpate a man's testicles to check for lumps or swellings, and examine the PENIS for structural anomalies or discharge. The familiar "turn your head and cough" instruction increases pressure in the lower abdomen to reveal any HERNIA. A woman's physical examination typically includes a PELVIC EXAMINATION and PAP TEST. Depending on age, the doctor may include a DIGITAL RECTAL EXAMINATION (DRE) for men and women.

Job positions with highly physical demands such as firefighter or police officer, school sports and athletic programs, return-to-work following injury, and certifications such as for aviation and nautical pilots are among the special circumstances that may require routine medical examinations. The physical examination and diagnostic procedures will include any additional tests to meet the requirements. Appendix X, "Immunization and Routine Examination Schedules," provides information about how frequently a person should have a routine medical examination and what components the examination should include.

See also HEALTH RISK FACTORS; LIFESTYLE AND HEALTH; OCCUPATIONAL HEALTH AND SAFETY.

S–Y

sexually transmitted disease (STD) prevention Doctors diagnose and treat about 12 million new STD infections annually in the United States, and more than 70 million Americans live with incurable STDs. Nearly all STD infections are preventable through sexual abstinence, which is a certain though often undesirable preventive measure, or through safer sex practices, which include using latex condoms with every sexual act and regular screening tests for STDs.

SEXUALLY TRANSMITTED DISEASES (STDs)

Curative Treatment	Treatment but No Cure
chancroid	GENITAL HERPES
CHLAMYDIA	HEPATITIS B
GONORRHEA	HIV/AIDS
lymphogranuloma venereum	HUMAN PAPILLOMAVIRUS (HPV)
nongonococcal URETHRITIS	
SYPHILIS	
TRICHOMONIASIS	

HEPATITIS C and TUBERCULOSIS also are often contracted through sexual contact though are not traditionally considered STDs. Untreated STDs can have significant health consequences including INFERTILITY, CENTRAL NERVOUS SYSTEM damage, generalized organ damage, and death. STDs can affect anyone who is sexually active. However, certain groups of people are more vulnerable to STD INFECTION and to the consequences of untreated STDs. Health experts classify these groups as special focus populations

- men who have sex with other men (MSM)
- injectable DRUG users
- men and women who have unprotected sex with multiple partners
- men and women entering correctional facilities
- adolescents and young adults
- women and infants

STDs may not cause symptoms, especially in women. A person who is unaware that he or she has an STD continues to spread the infection. The infection also has long-term personal consequences. For women, the key complication of untreated or repeated STD infection is PELVIC INFLAMMATORY DISEASE (PID), a leading cause of infertility. PID also can cause chronic PAIN and contribute to ECTOPIC PREGNANCY (also called tubal pregnancy), a life-threatening circumstance in which a pregnancy takes root in the fallopian tube or elsewhere in the abdominal cavity instead of the UTERUS.

Oral contraceptives (birth control pills), diaphragms, intrauterine devices (IUDs), and spermicides do not protect women from contracting STD infections.

Men may also have STDs without symptoms, though often develop urethritis (INFLAMMATION of the URETHRA) with discharge that leads to examination and diagnosis. In men and women alike, untreated SYPHILIS goes into stages of REMISSION. In most STDs, the infection remains contagious whether or not symptoms are present. The male latex condom is the most effective barrier against transmitting STDs. The pathogens that cause STDs cannot pass through the latex. However, contact between body fluids and mucous membranes can occur around the condom, so its protection is not foolproof. It is essential to use condoms properly (putting them on immediately upon erection and

before pre-ejaculate appears) and consistently for maximum preventive benefit.

Infants whose mothers have active STDs, particularly GONORRHEA and CHLAMYDIA, during delivery are at great risk for blindness. Hospitals routinely put antibiotic drops in the eyes of all newborns as a prophylactic measure. Infants born to HIV-positive mothers are also at risk for acquiring the VIRUS during birth; prophylactic medications such as azidothymidine (AZT) can help thwart infection.

The US Centers for Disease Control and Prevention (CDC) has a national STD/HIV hotline available 24 hours a day, 7 days a week, for questions and information: 800-227-8922

Prevention efforts focus on education about STDs and their potential health consequences in combination with appropriate methods to reduce the likelihood of infection. The most effective prevention method is abstinence from sexual activity, or, when sexually active, sex exclusively within a monogamous relationship. Because some STDs may be present without symptoms in up to 70 percent of people infected, health experts recommend routine screening for all sexually active individuals as a preventive measure to help contain the spread of infection.

KEY MEASURES FOR PREVENTING STDS

- Use a latex condom for every sexual act.
- Restrict sexual activity to a monogamous relationship.
- Receive regular screening tests for STD infection.

See also CONTRACEPTION; HEALTH RISK FACTORS; LIFESTYLE AND HEALTH; YOUTH HIGH-RISK BEHAVIOR.

sick building syndrome A set of symptoms that appear when in a particular building and go away upon leaving the building. The US Environmental Protection Agency (EPA) defines sick building syndrome as symptoms that

- include HEADACHE, NAUSEA, itchy eyes and NOSE, and dry COUGH
- doctors cannot diagnose as any specific health condition
- are present only when within the building

Symptoms may affect a few people in a particular area or numerous people throughout the building. Because symptoms often are general and are present only when the person is in the building, obtaining a diagnosis of illness is challenging. Sometimes symptoms improve with ANTIHISTAMINE MEDICATIONS to combat allergic response, though most people do not want to take medications for symptoms they can relieve by being in a different location.

The causes of sick building syndrome are unclear though scientists believe they may relate to INDOOR AIR QUALITY, chemicals in the air from indoor or outdoor sources such as exhaust fumes or glues, contaminants such as molds or fungi that cause allergy-like reactions, and inadequate ventilation. Increased ventilation (higher turnover of air volume) and air-filtration systems may improve indoor air quality sufficiently to mitigate symptoms for most people. Some individuals may have heightened sensitivity to airborne substances.

See also ALLERGIC RHINITIS; BUILDING-RELATED ILLNESS; ENVIRONMENTAL CIGARETTE SMOKE; OCCUPATIONAL HEALTH AND SAFETY.

substance abuse prevention SUBSTANCE ABUSE is a complex health and social problem with public health as well as personal health consequences. Accordingly, substance abuse prevention efforts require coordinated efforts that align individuals, parents, schools, employers, and health-care providers toward common goals. Though education is the cornerstone of substance abuse prevention, it is naive to believe education alone is sufficient to stop a person from trying or using TOBACCO, ALCOHOL, drugs, and illicit substances. Many knowledgeable people have substance abuse problems.

Parents, teachers, sports figures, and other adults significantly influence the attitudes and actions of children. Adults who do not smoke or use illicit drugs and who use alcohol and medications appropriately and responsibly help model attitudes and behaviors that discourage substance abuse. Focused prevention efforts target underage smoking and drinking, emphasizing abstaining

from both. Other efforts attempt to address issues of ADDICTION through treatment programs.

KEY MEASURES FOR PREVENTING SUBSTANCE ABUSE

- education through schools and community outreach regarding the health risks of substance abuse
- effective and appropriate modeling by adults
- access to treatment programs
- take medications, over-the-counter or prescription, only as needed and directed
- restrict underage access to TOBACCO, ALCOHOL, and medications of abuse

See also ALCOHOLISM; OVERDOSE; SMOKING CESSATION; TOLERANCE.

sudden infant death syndrome (SIDS) The unexpected and unexplainable death of an infant under age one year, most commonly between the ages of two and four months. Researchers do not know what causes SIDS, though believe a malfunction occurs in the infant's basic metabolic regulatory mechanisms that allows BLOOD PRESSURE, BREATHING, and body temperature to fluctuate. Also for reasons researchers do not understand, SIDS is three times more frequent among African American and Native American infants. SIDS is also more likely to occur among infants whose mothers are under age 20 years, smoke, gain inadequate weight during PREGNANCY, or have pregnancies less than a year apart.

Infants who sleep on their backs have a significantly lower rate of SIDS than infants who sleep on their sides or stomachs, prompting the national "Back to Sleep" campaign in 1994 to lower the risk for SIDS. Deaths due to SIDS dropped almost in half in subsequent years. Because researchers do not know why SIDS occurs, however, they are not certain how, or whether it is possible, to prevent it.

Because the infant's death is sudden and unexplained, local authorities must investigate. This adds to the emotional trauma for families because it is a difficult experience to undergo and even when SIDS is the conclusion, the question of why often remains unanswered. Inasmuch as the causes of SIDS remain unclear, health and law-enforcement experts do know that SIDS is *not* the result of parental neglect or CHILD ABUSE. Infants born prematurely and those whose mothers smoked during pregnancy appear to have higher risk for SIDS. Pediatricians may recommend special monitors for especially vulnerable infants that sound an alarm when the infant's breathing rate or body temperature becomes higher or lower than normal.

KEY MEASURES FOR PREVENTING SIDS

- Place infant on his or her back to sleep, not on the side or STOMACH.
- Place infant to sleep in his or her own crib.
- Maintain the infant's room at a temperature warm enough to allow sleeping without blankets but not hot.
- Keep heavy blankets, quilts, and stuffed animals out of the infant's crib.
- Maintain a smoke-free living environment and prevent exposure to cigarette smoke in general.

See also NERVOUS SYSTEM; PRENATAL CARE.

trauma prevention Firearms, MOTOR VEHICLE ACCIDENTS, SEXUAL ASSAULT, DOMESTIC VIOLENCE, CHILD ABUSE, workplace and school VIOLENCE, animal bites, and major falls account for the majority of traumatic injuries. As is the case with other kinds of ACCIDENTAL INJURIES, most traumatic injuries are preventable. Traumatic injuries have a high likelihood of death within the first several hours after the events responsible for them, and require emergency medical treatment. Traumatic injuries

KEY MEASURES FOR PREVENTING TRAUMA

- Use trigger locks and gun safes to store guns, and separate guns from ammunition.
- Take firearms safety classes before hunting or target shooting, and always handle a gun as though it were loaded.
- Wear seat belts at all times when traveling in a motor vehicle and helmets when riding on a motorcycle, whether the driver or a passenger.
- Wear or use appropriate safety gear when using power tools and performing home repairs, and for recreational activities such as rock climbing.
- Stabilize ladders and do not step higher than recommended onto a stepladder or ladder.
- Keep dogs leashed or fenced, and do not approach wild animals.
- Seek professional help for anger management and DOMESTIC VIOLENCE issues

also account for a significant percentage of long-term recovery and permanent disability due to injury. Prevention efforts focus on increasing public awareness and reducing exposure to risks.

See also ANGER AND ANGER MANAGEMENT; BLUNT TRAUMA; GUNSHOT WOUNDS; MULTIPLE TRAUMA; OCCUPATIONAL HEALTH AND SAFETY.

tuberculosis prevention Until researcher Selman Waksman (1888–1973) discovered the powerful antibiotic streptomycin in 1944, TUBERCULOSIS (called "consumption" because its sufferers literally wasted away as the INFECTION consumed lung and other tissue) killed more people than any other disease. Antibiotic regimens developed in the ensuing decade significantly reduced tuberculosis infections in the United States by the mid-1960s. By the mid-1980s, however, strains of tuberculosis began appearing that were resistant to the conventional antibiotic therapy (now called multidrug-resistant tuberculosis or MDR-TB). Concurrently HIV/AIDS proliferated, making those who became infected highly susceptible to other infections such as tuberculosis. People who have DIABETES, kidney disease, LEUKEMIA, or LYMPHOMA or who receive IMMUNOSUPPRESSIVE THERAPY such as following ORGAN TRANSPLANTATION are also more susceptible to tuberculosis infection. Tuberculosis tends to develop more frequently among confined populations such as in prisons and crowded living conditions.

Doctors diagnose about 15,000 people with tuberculosis in the United States each year, about half of whom are immigrants who likely became infected in their native countries. Tuberculosis spreads by BREATHING droplets a person already infected with the disease breathes or coughs out into the air. Most people who have healthy immune systems can fight off infection, though the causative microorganism (*Mycobacterium tuberculosis*) may remain inactive in their bodies (called latent tuberculosis). Only people who have active tuberculosis can spread the infection to others. A SKIN test can detect the presence of *M. tuberculosis*. Public health policy in the United States requires skin testing, called a tuberculin skin test, in numerous occupations including public safety (police, fire, and emergency aid response), teaching, food handling and preparation, and health care. The typical course of treatment for diagnosed active tuberculosis is a regimen of two or more ANTIBIOTIC MEDICATIONS taken for 6 to 10 months.

Prevention efforts focus on screening susceptible populations for early diagnosis and treatment, and on encouraging people who show symptoms of tuberculosis to receive medical treatment. Anyone who has had close contact with a person diagnosed with tuberculosis, as well as those who have HIV/AIDS and a marginal tuberculin skin test result should receive more frequent screening tests and discuss prophylactic antibiotic therapy with their doctors. Research continues the quest for a tuberculosis VACCINE. The BCG vaccine currently available provides very limited protection. Doctors administer it primarily to young children exposed to non-lung forms of tuberculosis infection.

KEY MEASURES FOR PREVENTING TUBERCULOSIS

- Receive periodic tuberculin SKIN tests to screen for the presence of *M. tuberculosis*.
- Receive prophylactic antibiotic therapy when at high risk for INFECTION.
- Take protective measures such as wearing a surgical mask when in close contact with someone diagnosed with tuberculosis.
- If being treated for tuberculosis, take the full course of antibiotic therapy as prescribed.

See also KIDNEYS; LUNGS; OCCUPATIONAL HEALTH AND SAFETY.

water safety More than 4,000 people drown in the United States each year, and as many as 12,000 experience near-drowning (also called submersion injury). The HYPOXIA (lack of oxygen) that occurs with submersion results in residual complications in about 40 percent of people who are revived, ranging from mild memory impairment and disturbances of cognitive function to PERSISTENT VEGETATIVE STATE. Virtually all water accidents are preventable.

The common scenarios for water-related injuries correlate with age:

- Children under age 1 year are most likely to drown in toilets, bathtubs, and buckets or other containers of water.

- Children between the ages of 1 and 4 years are most likely to drown in residential swimming pools.
- Young people between the ages of 15 and 19 are most likely to drown in lakes and rivers, and ALCOHOL consumption contributes up to half of their water-related injuries and deaths.
- Boating accidents are the most common cause of submersion injuries among adults. Alcohol consumption is a factor in nearly half of such accidents.
- Among adolescents and adults, diving into shallow water accounts for numerous HEAD AND SPINAL CORD INJURIES.

Three of four people who drown are adults. Even capable swimmers can experience exhaustion, MUSCLE cramps, and other challenges. Many people who die in boating accidents are not wearing personal flotation devices (PFDs) or lack other water safety devices that could have prevented their deaths. Alcohol consumption and swimming or boating factors in about 40 percent of water-related injuries among adolescents and adults.

KEY MEASURES FOR PREVENTING DROWNING

- Learn to swim.
- Learn CARDIOPULMONARY RESUSCITATION (CPR).
- Wear or use appropriate flotation devices when engaged in water activities such as boating.
- Closely supervise children in and near water, including pools, lakes, and rivers.
- Do not drink ALCOHOL when participating in activities on or in the water.

See also COLD WATER DROWNING; HYPOTHERMIA; SPINAL CORD INJURY; TRAUMATIC BRAIN INJURY (TBI); WARM WATER DROWNING.

youth high-risk behavior The US Centers for Disease Control and Prevention's (CDC's) Youth Risk Behavior Surveillance System (YRBSS) monitors behaviors among young people that can adversely affect their health. Key areas of focus include TOBACCO use, substance abuse, sexual activity, PREGNANCY, violent behavior, ACCIDENTAL INJURIES, physical inactivity, EATING HABITS, and attempted suicide. YRBSS data help public health organizations develop intervention strategies and programs to reduce adverse health consequences among youth. The CDC surveys students in middle schools and high schools throughout the United States to collect YRBSS data.

HIGH-RISK HEALTH BEHAVIORS AMONG YOUTH

anabolic steroid use	binge drinking
carrying a weapon	cigarette smoking
does not drink milk	does not eat fruit, vegetables
drinking and driving	failure to wear bike helmet
fast food consumption	fighting
ILLICIT DRUG USE	lack of seat belt use
laxatives or diet aids to lose weight	multiple sex partners
nonsmoking TOBACCO use	no regular physical exercise
overweight or obese	regular ALCOHOL consumption
riding with intoxicated driver	sexual activity without a condom
suicide ideation or attempts	

See also LIFESTYLE AND HEALTH; HEALTHY PEOPLE 2010.

ALTERNATIVE AND COMPLEMENTARY APPROACHES

The current time is one of a paradigm shift in the nature and delivery of health care that affects everyone—researchers, patients, doctors, and insurers—alike. Tremendous discoveries in medicine are leading to a reexamination of attitudes and practices across the spectrums of health and of disease. As conventional medicine intensifies its focus on lifestyle management and preventive measures and on viewing the patient as a "whole" person (the holistic view common to many alternative and complementary health systems), both doctors and individuals are finding therapeutic value in incorporating many alternative and complementary therapies within integrative treatment plans.

This section, "Alternative and Complementary Approaches," presents an overview discussion of treatment approaches that are beyond the boundaries of conventional medicine yet still within the realm of which conventional doctors may responsibly include them as elements of integrative treatment plans. The entries that follow represent the range of the alternative and complementary therapies available from ancient healing systems, such as TRADITIONAL CHINESE MEDICINE (TCM) and AYURVEDA, to MEDICINAL HERBS AND BOTANICALS. As well, several entries present methods that are controversial and potentially hazardous from the conventional medicine perspective, such as CHELATION THERAPY. Such entries are included not to give them credibility but because widespread misperceptions about them persist despite a clinically valid body of knowledge that supports concerns about their risks.

Context and Perspective

This section presents the discussion of alternative and complementary approaches within the context and perspective of conventional medicine as practiced in the United States, as this is the orientation of *The Facts On File Encyclopedia of Health and Medicine*. Some conventional doctors share the interest and enthusiasm of patients who want to incorporate alternative and complementary therapies, and some conventional doctors are less willing to entertain such inclusions. Much depends on the convergence of the patient's interests and condition with the doctor's knowledge and trust in specific alternative and complementary therapies. The efficacy of some ancient healing systems and methods is perhaps more trustworthy than that of isolated or obscure practices. The challenge for doctors and patients alike is to evaluate what bodies of knowledge exists about popular therapies, to understand which of them may have therapeutic value.

Most alternative therapies derive from healing systems deeply rooted in philosophical frameworks that differ dramatically from those of conventional Western medicine. A conventional physician's training does not include most of these methods, even the most studied or popular ones. Doctors must instead rely on evaluating the available research to determine whether, how, and when alternative and complementary approaches are appropriate in conjunction with conventional care. For some methods, not much data are available. As knowledge about these approaches increases, many conventional doctors may be more confident about incorporating them. Indeed, some conventional doctors seek additional education and certification in alternative and complementary therapies such as ACUPUNCTURE and herbalism so they can offer their patients a broader spectrum of therapeutic and preventive options.

The conventional framework that guides the practice of medicine in the United States is physician centered and based in measurable evidence and reliably repeatable results through controlled clinical studies. Though the true measure of a treatment's success is whether people improve or worsen with its use, evidence-based standards give conventional physicians a sense of reasonable expectation when making treatment decisions and recommendations. Many conventional doctors are increasingly interested and willing to add responsible alternative and complementary therapies to integrative treatment plans when they have reasonable expectations for how such therapies may benefit the patient's condition or QUALITY OF LIFE.

When looking at the broad range of alternative and complementary approaches from acupuncture to PRAYER AND SPIRITUALITY to VISUALIZATION it is also important to understand how patients look to these methods in preventive and lifestyle contexts. MEDITATION and YOGA, for example, have become fairly mainstream as practices to reduce stress and are gaining acceptance for their abilities to influence health conditions such as HYPERTENSION (high BLOOD PRESSURE). As researchers and doctors learn more about the pathways and mechanisms of MIND–BODY INTERACTIONS, they understand more fully how lifestyle and preventive health measures, with a holistic view of the individual, are important. Within such a context, yoga and exercise become comparable complements to good health. Whether one or the other is "alternative" or "conventional" has little relevance; each benefits health in similar ways.

COMMON ALTERNATIVE AND COMPLEMENTARY THERAPIES

ACUPUNCTURE	AROMATHERAPY
ART THERAPY	BIOFEEDBACK
Chinese herbal remedies	CRANIOSACRAL MASSAGE
FLOWER ESSENCES	HYPNOSIS
MAGNET THERAPY	MASSAGE THERAPY
MEDICINAL HERBS AND BOTANICALS	NUTRITIONAL THERAPY
OSTEOPATHIC MANIPULATIVE TREATMENT (OMT)	PRAYER AND SPIRITUALITY
	TAI CHI
VISUALIZATION	VITAMIN AND MINERAL THERAPY
YOGA	

Historical Traditions in Alternative Healing Systems

The oldest known healing systems still in practice today, traditional Chinese medicine (TCM) and Ayurveda, date to perhaps 3000 B.C.E., well before the advent of written language. NATIVE AMERICAN HEALING originating among the indigenous cultures of the North American continent melds spirituality and health in much the same fashion as does India's Ayurveda and, archaeological evidence suggests, could have origins that are nearly as ancient. In these systems, healers passed their knowledge from one to another, generation to generation, through tradition and experience. In some cultures each successive generation developed improvements on the methods of healing their ancestors used, and in other cultures each generation of healers practiced in precise compliance with the traditions they learned from the generations before them.

Some alternative healing systems are relatively modern, emerging within the past 100 or 200 years as outgrowths of what were the medical practices of their times. Though common perception views alternative and complementary therapies as Eastern in their philosophies and practices, these newer systems—notably HOMEOPATHY, NATUROPATHY, and OSTEOPATHY—are Western in origin and orientation. One alternative healing method, CHIROPRACTIC, is uniquely American.

ALTERNATIVE HEALING SYSTEMS

AYURVEDA	HOMEOPATHY
NATIVE AMERICAN HEALING	NATUROPATHY
OSTEOPATHY	TRADITIONAL CHINESE MEDICINE (TCM)

Interest in, and use of, alternative therapies is a growing phenomenon in the United States. According to a 2002 survey by the US National Center for Complementary and Alternative Medicine (NCCAM) and the US Centers for Disease Control and Prevention (CDC) National Center for Health Statistics (NCHS), nearly two thirds of Americans use some form of alternative health practice, most of them to complement their conventional medical care.

Surveys show that half choose alternative therapies on their own to complement conventional therapies, a quarter use alternative therapies their

conventional physicians recommend, and a quarter use alternative therapies on their own because they believe conventional medicine will not help their conditions. Nearly 12 million Americans seek relief from BACK PAIN alone through alternative and complementary therapies (excluding prayer). Other common uses of alternative and complementary therapies (excluding prayer) include arthritis and JOINT PAIN, chronic HEADACHE, FIBROMYALGIA, anxiety and DEPRESSION, chronic gastrointestinal conditions, hypertension, and MENOPAUSE discomfort. Many people use alternative and complementary therapies to provide relief during cancer treatment and from cancer symptoms.

NCCAM/NCHS 2002 SURVEY'S TOP 10

Alternative/Complementary Practice	Percentage of Americans Who Use
prayer specifically for one's own health	43.0 percent
prayer by others for one's health	24.4 percent
natural products	18.9 percent
deep BREATHING EXERCISES	11.6 percent
participation in prayer group for one's own health	9.6 percent
MEDITATION	7.6 percent
CHIROPRACTIC care	7.5 percent
YOGA	5.1 percent
massage	5.0 percent
diet-based therapies	3.5 percent

Source: Barnes, P; Powell-Griner, E; McFann, K; and Nahin, R. CDC Advance Data Report #343. Complementary and Alternative Medicine Use Among Adults: United States, 2002. *May 27, 2004.*

"First, Do No Harm"

Alternative and complementary approaches often draw people to try them on their own, without consulting their conventional doctors. People may be curious about certain methods, frustrated or disappointed with the results of conventional treatments, or have limited access to conventional health care. In choosing from alternative and complementary therapies, it is prudent to learn as much as possible about the method so as to "first, do no harm" as the time-honored medical dictum cautions. And, when possible, seek the advice of a conventional doctor to gain perspective to what often is confusing or conflicting information.

Though it is seldom harmful to drink GREEN TEA, do yoga, or have REIKI, some alternative and complementary methods may be hazardous as may be some conventional methods—for people who have certain health conditions. For example, people who have RHEUMATOID ARTHRITIS or other degenerative musculoskeletal disorders may risk serious injury with craniosacral therapy, OSTEOPATHIC MANIPULATIVE TREATMENT (OMT), or chiropractic manipulation. NUTRITIONAL THERAPY may alter medication needs for people who have DIABETES, MALABSORPTION disorders, or conditions affecting the LIVER or KIDNEYS. It is important to choose the most reliable and credible methods and practitioners, and to coordinate care among all the providers involved in its delivery, conventional and complementary.

Using alternative and complementary approaches in coordination with conventional treatments may alleviate some symptoms but cannot effectively substitute for conventional medical care for many health conditions ranging from HYPOTHYROIDISM TO CANCER.

For people who are undergoing conventional medical treatment such as CHEMOTHERAPY or RADIATION THERAPY, it is worthy to ask doctors what to eat, how and when to exercise, and what measures can support health; the environment of the body changes dramatically during such therapies, and sometimes approaches that are supportive and complementary to the conventional treatment can lessen the harshness of the experience. For many circumstances, however, available information fails to provide clear answers and it becomes a matter of trusting the doctor and making common sense decisions.

Science Meets Tradition: Evidence and Standards

Scientific evidence is scarce for many alternative and complementary therapies. Many therapies have evolved over centuries of use and produce reliable results even though contemporary clinical science cannot yet explain the mechanisms of the method. Acupuncture, for example, has been an integral component of TCM, as well as other healing systems, for several thousand years. At

acupuncture's foundation, within these systems, is the presence of an extensive network of energy channels, called meridians, in the body. Though these meridians are not tangible, perceptible structures in the conventional sense, they are nonetheless a centuries-old map of energy pathways in the body. That contemporary researchers have yet to quantify them does not necessarily invalidate their existence. Indeed, not until the invention of devices such as the microscope in the eighteenth century, and really not until its application in exploring the structure of the human body in the nineteenth century, did scientists discover the networks of nerves that convey information and instructions from the BRAIN to each cell in the body. Medical science is ever-evolving, and new technologies continually reveal new and paradigm-shifting discoveries (such as mapping the human genome).

Herbal remedies and medicinal foods contain numerous potentially active ingredients. Conventional clinical studies of the intact substance, such as the soybean, may yield different results than studies of the substance's known active ingredients, such as SOY isoflavones. A substance may appear to be a "heal-all," raising questions about PLACEBO effect. And yet the substance may simply have such broad-reaching actions in the body, such as stimulating the immune system, that it truly does have healing effects for numerous health conditions.

Evidence of effectiveness and mechanism of action may be in short supply simply because the clinical research studies that are today the foundation of conventional medicine may not have investigated a particular therapy or may have produced inconclusive findings. Sometimes multiple studies generate conflicting data. Some methods have been copiously studied, though according to standards other than those common in the United States. And, of course, numerous "therapies" are available that have dubious therapeutic value (and may appear clearly ineffective or even harmful) and have no foundation within the context of any healing system.

As a result of these mixed circumstances, there is considerable disagreement among conventional doctors and clinical scientists about the effectiveness and potential risks of many alternative and complementary therapies. These possibilities apply as well to conventional therapies. Researchers do not fully understand the mechanisms of many drugs, such as levodopa to treat PARKINSON'S DISEASE, the tricyclic ANTIDEPRESSANT MEDICATIONS, and many of the medications doctors prescribe to treat HEART conditions. However, empirical evidence (observable, reproducible effects) support their effectiveness to the extent that conventional doctors are comfortable using them. Such is becoming the case with some alternative and complementary approaches that lend themselves to empirical study, such as acupuncture.

As the current health-care paradigm continues to change, it is natural to expect conflicting viewpoints about the best standard of care to emerge. Until there is a truly integrated approach, there will be a higher level of responsibility on the individual to participate in health-care decisions and to choose care that is wise and effective. This applies as much to the choice to use acupuncture as to enroll in a clinical study for an experimental drug or treatment.

Breakthrough Research and Treatment Advances

Advances in medical technology, particularly imaging procedures, have made possible the study of alternative and complementary therapies in ways that allow researchers to explore how they alter physiologic functions. POSITRON EMISSION TOMOGRAPHY (PET) SCAN and MAGNETIC RESONANCE IMAGING (MRI), for example, allow researchers to observe, in real time, the changes that take place in the brain and other parts of the body with therapies such as HYPNOSIS, acupuncture, MEDITATION, visualization, and even prayer. Numerous studies underway are investigating alternative therapies such as botanical and herbal remedies to relieve the discomforts of menopause, CANCER and CARDIOVASCULAR DISEASE PREVENTION and treatment claims, methods for pain management, and mind–body interventions to mitigate the symptoms of chronic health conditions.

The current health-care culture is reaching for new understanding that can unify technology, conventional techniques, and complementary methods in a single, amazing paradigm for treatment of the human being in health and in illness. Within this paradigm is the potential for many of

the complementary approaches to be as "conventional" in their use and application as advances in technology such as GENE THERAPY, molecular medicine, diagnostic imaging, ORGAN TRANSPLANTATION, BIOLOGICAL RESPONSE MODIFIER, and PHARMACOGENOMICS.

Even today, hospitals are quietly becoming models of such an integrative paradigm. Neonatal intensive care units employ MASSAGE THERAPY and music therapy to soothe the fragile premature infants born before their bodies and systems developed fully. Patients waiting for organ transplants or undergoing high-tech cancer treatments receive instruction in meditation and visualization. Reflection gardens, labyrinths, Native American prayer wheels, meditation rooms, and chapels provide quiet, calming environments for prayer and contemplation.

This is a time of record breakthroughs in medical discoveries. Researchers are exploring more and more experimental treatments, conventional as well as alternative and complementary. Keeping up with the incredible pace of new knowledge challenges doctors and individuals alike. What is clear already is that as knowledge increases, the best care will be that which presents an informed integrative approach guided by progressive conventional doctors based on individual patient needs, using the simplest, most effective methods for restoring and maintaining health.

A

acupuncture A HEALING method in which the acupuncturist inserts hair-thin needles into the body at various locations along energy channels called meridians. The underlying premise is that disease represents imbalances of the flow of energy (chi), and the needles redirect the flow to restore balance and thus health. The practice of acupuncture dates back at least 2,500 years to the origins of TRADITIONAL CHINESE MEDICINE (TCM), and today remains an integral component of TCM.

The Western adaptation of acupuncture views the practice primarily from the perspective of PAIN relief and shifts the underlying mechanism to one in which the needles stimulate NERVE endings, eliciting biochemical and electromagnetic responses that interrupt the flow of pain messages to the BRAIN. Another Westernization of acupuncture is electrostimulation of the acupuncture needles after inserting them, which intensifies the effect.

COMMON THERAPEUTIC APPLICATIONS OF ACUPUNCTURE

ADDICTION	ASTHMA
BACK PAIN	CARPAL TUNNEL SYNDROME
CHEMOTHERAPY nausea	CHRONIC FATIGUE SYNDROME
CONVERT BREECH PRESENTION IN PREGNANCY	dental PAIN
FIBROMYALGIA	ENDOMETRIOSIS
INDUCE LABOR IN PREGNANCY	HEADACHE
menopausal HOT FLASHES	IRRITABLE BOWEL SYNDROME (IBS)
menstrual cramps	motion sickness
OSTEOARTHRITIS	POLYCYSTIC OVARY SYNDROME (PCOS)
postoperative NAUSEA	RELIEVE NAUSEA AND VOMITING
PREMENSTRUAL SYNDROME (PMS)	SMOKING CESSATION
ROTATOR CUFF IMPINGEMENT SYNDROME	tennis elbow (EPICONDYLITIS)
sports injuries	

Numerous clinical studies of acupuncture have provided evidence that acupuncture does indeed relieve pain. However, no study has yet been able to identify the precise mechanisms by which relief takes place. In 1997 the US National Institutes of Health (NIH) issued a consensus statement acknowledging the primary therapeutic value of acupuncture for a variety of health situations and conditions such as NAUSEA, HEADACHE, dental pain, OSTEOARTHRITIS, and ADDICTION. This marked the turning point for acceptance of acupuncture as a mainstream treatment option for numerous health conditions.

The Acupuncture Experience

Most people find the experience of acupuncture relaxing, calming, and even somewhat euphoric. The hair-thin needles are so fine that they are difficult to see; most people do not feel them when the acupuncturist inserts them. The acupuncturist first directs the person to lie on a padded table or sit in a recliner-style chair, depending on the location of the acupuncture points and reason for treatment, and then inserts the needles. After insertion, the needles stay in place for 20 to 30 minutes. Occasionally a needle falls out; this is okay and does not affect the treatment.

Some conditions need only 2 or 3 treatments, usually about a week apart. Other conditions may require up to 10 or 12 weekly treatments for relief and occasional follow-up treatments for maintenance. For aural, or earlobe, acupuncture to treat addiction or for SMOKING CESSATION, the acupuncturist may place a small needle, like a button, leaving it in place until it falls out on its own hours to days later.

In the United States acupuncturists must use single-use, disposable needles to prevent the

spread of bloodborne infections such as HEPATITIS and HIV/AIDS. Though adverse effects are rare, they can occur. Some people experience continued tingling at the site of a needle insertion, and occasionally there is very minor bleeding at a needle site. People who are uncomfortable with the thought or sight of needles may choose to close their eyes when the acupuncturist is handling and inserting needles. One of the most common side effects of acupuncture, typically among people who are new to the procedure, is fainting at the sight of a needle or when the acupuncturist inserts the first few needles. Such a response relates to the person's fear or concern about the procedure, not the acupuncturist's technique.

Choosing an Acupuncturist

Most acupuncturists in the United States are health-care practitioners such as conventional doctors (MDs and DOs), naturopathic doctors (NDs), chiropractors (DCs), and dentists (DDSs or DMDs). Most states have some level of certification or licensing, though standards are inconsistent among states. The minimum education and training required for MDs and DOs to become a licensed acupuncturist in the United States is 200 hours. Some states extend this requirement to NDs and DCs. States that will license an acupuncturist who is not a trained health professional typically require completion of an accredited acupuncture program that is about 3,000 hours of classroom education and experiential training. A licensed acupuncturist uses the designation L.Ac. after his or her name.

Because standards vary among states, health experts recommend obtaining recommendations and referrals for acupuncturists, especially for people who are new to acupuncture. As with any health-care practitioner, it is important to feel comfortable with, and to trust, the acupuncturist.

See also ALTERNATIVE METHODS FOR PAIN RELIEF; BIOFEEDBACK; MIND–BODY INTERACTIONS; OSTEOPATHIC MANIPULATIVE TREATMENT; REFLEXOLOGY; TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION.

anti-aging approaches It is a common observation that people who fully engage in the activities of living from when they wake in the morning until they go to bed at night seem to be much younger than their chronological ages. They look younger, they act younger, they feel younger. With longevity continuing to increase, many people are searching for ways to be among those who seem young. It is enticing to think such efforts might be as simple as taking a pill every morning. While some methods to maintain the health and vigor of youth show intriguing promise, many are ineffective or potentially harmful.

Aging Interventions

Products marketed to slow the aging process seldom can substantiate their claims through clinical studies and objective measures. Nonetheless, they are appealing because everyone wants to believe they can work. And some may be helpful, though researchers do not yet know. Some products commonly marketed as anti-aging substances include

- Hormones such as DEHYDROEPIANDROSTERONE (DHEA) (a TESTOSTERONE/estrogen precursor the adrenal glands produce) and human GROWTH HORMONE (hGH), which marketers claim reverse aging effects such as lost MUSCLE mass and BONE DENSITY. Some clinical studies show these hormones can indeed have such effect. However, health experts caution that there are as yet no studies that evaluate the effects and consequences of these products over the long term.
- Antioxidants such as vitamins and COENZYME Q10, marketed as substances that can clean up the molecular waste that otherwise accumulates to cause disease. Indeed, antioxidants do bind with free radicals, molecular particles that remain in cells as byproducts of energy generation. What is much less clear is the precise role free radicals have in causing diseases such as DIABETES, CANCER, CARDIOVASCULAR DISEASE (CVD), OSTEOARTHRITIS, PARKINSON'S DISEASE, and other health conditions typically associated with aging.

Conventional health experts believe there is little value to claims about any products that say they can stop or reverse the aging process. Though such claims remain out there, the bigger truth also remains: None of these products ever kept anyone

from growing older or from eventually reaching the end of his or her lifetime.

Healthy Aging

In the mid-1990s researchers at the Tufts University Center for Aging compared two groups of women ages 50 to 70. At the start of the study, the women in both groups were all sedentary. One group stayed that way. The other group participated in progressively intense physical STRENGTH training. At the end of 1 year the women in the strength training group looked, felt, and acted 20 years younger than the women in the sedentary group. Other studies involving other groups have shown, too, that people who stay physically and mentally active experience fewer illnesses and injuries, and maintain cognitive ability and memory function.

Many health experts believe the true "fountain of youth" is within each individual and the lifestyle choices he or she makes. Of course no one chooses to be sick. In fact, illness 40 years down the road is not what most people think about when making choices about eating, exercise, and smoking. Yet many of the choices people make lead to the chronic health conditions that have come to characterize growing older in America. Though not as glamorous as pills that promise to turn back the calendar, doing what is possible to contain the risks for these conditions, many health experts say, is the one anti-aging approach in which anyone and everyone can participate.

See also ESTROGENS; HEALTH RISK FACTORS; HORMONE; HUMAN GROWTH HORMONE (HGH) SUPPLEMENT; LIFESTYLE AND HEALTH; QUALITY OF LIFE.

aromatherapy The therapeutic use of essential oils of plants delivered via the sense of smell. Essential oils are highly concentrated liquid extracts from the stems, leaves, flowers, and other parts of plants that contain the energy essence of the plant. Aromatherapy is a form of energy HEALING always done to complement or accompany other therapeutic forms. A qualified aromatherapist can mix personalized blends as recipes to meet a person's individual needs. In the United States essential oils are available in health food stores, and many major grocery stores and drugstores carry common oils that anyone can buy.

COMMON ESSENTIAL OILS FOR AROMATHERAPY

Essential Oil	Therapeutic Use
anise	upper respiratory INFECTION
basil	focus and concentration
cedarwood	arthritis
citrus	mental clarity and alertness
eucalyptus	congestion
jasmine	DEPRESSION
lavender	anxiety, insomnia
peppermint	NAUSEA relief
rose	relaxation, gastrointestinal upset, dry SKIN
rosemary	MUSCLE relaxation
sandalwood	stress
thyme	circulation
vanilla	confidence, relaxation
ylang-ylang	anxiety, PALPITATIONS, stress

The most common method for dispensing an essential oil is diffusion, in which a heat source such as a candle or low-watt light bulb warms a solution of water and the essential oil. Often the essential oil also carries the fragrance of the plant, giving off a pleasant smell. However, according to the principles of aromatherapy, it is the energy nature of the essential oil, not necessarily its fragrance, that provides therapeutic benefit. Fragranced solutions that are not essential oils may smell no different but aromatherapists contend they have no therapeutic value.

Many alternative and complementary practices integrate aromatherapy, which health experts consider to be mostly safe. Some essential oils can stimulate physiologic changes in the body that may be hazardous during PREGNANCY; pregnant women should discuss using aromatherapy with their obstetricians or midwives. The essential oils for aromatherapy are for external use only. Most are harmful, and some can be fatal, if ingested. Many essential oils are irritating to the SKIN unless significantly diluted with neutral carrier oils (such as almond oil) before application.

See also FLOWER ESSENCES; HOMEOPATHY; MEDITATION; PRAYER AND SPIRITUALITY; VISUALIZATION.

art therapy A HEALING approach that uses the creative arts to help people, especially children, express suppressed emotions. Art therapy may employ drawing, writing, dancing, singing, drama, painting, storytelling, sculpting with clay, and

other forms that allow free and creative expression. The underlying philosophy of art therapy is that the processes of creativity are also pathways of insight and understanding. With focused exploration of the art a person creates, he or she can gain new perspectives and learn to solve problems or reconcile situations that cause stress, anxiety, or DEPRESSION.

Art therapists typically have either a graduate degree in art therapy or dual graduate degrees in art and psychology (or related fields). A registered art therapist meets the education and experience requirements of the Art Therapy Credentials Board. In the United States, each state regulates the licensing requirements for art therapists. Art therapists may work in hospitals, health-care clinics, rehabilitation centers, and private practice.

See also COGNITIVE THERAPY; GENERALIZED ANXIETY DISORDER (GAD); MIND–BODY INTERACTIONS.

Ayurveda A philosophy of HEALING based in ancient Hinduism that dates perhaps to 4500 B.C.E. or earlier. Ayurveda considers all of existence in the context of energy, including human beings. Each person represents the essential elements of universal energy (fire, air, water, earth, and ether), which manifest in three states of physical existence called *doshas: vata, pitta,* and *kapha.* Health exists when there is balance among the *doshas,* and illness (or ailment) represents imbalance. The *dosha*'s association indicates the general nature of the ailment. BACK PAIN, for example, represents a *vata* imbalance (movement) and indigestion is a *kapha* imbalance (structure).

Ayurvedic Diagnosis and Treatment

Key to the Ayurvedic diagnostic process is careful assessment of the tongue and the six pulses of each arm, three superficial and three deep. The pulses provide information about the balances and imbalances in the *doshas*. The Ayurvedic practitioner asks many questions about the individual's health, health concerns, family, lifestyle, and life in general. Ayurvedic therapies attempt to restore *dosha* balance through herbal remedies, YOGA poses, dietary changes, and lifestyle measures.

AYURVEDIC DOSHAS

Dosha	Elemental Energy	Association
vata	ether (space) and air	movement
pitta	fire	transformation
kapha	earth and water	structure

Ayurvedic Practitioners

In India, Ayurvedic practitioners train for five to six years before going into practice on their own. A US-trained Ayurvedic practitioner completes a one-year program of study and then can practice. There are no licensing education or requirements for Ayurvedic practitioners in the United States. Some alternative health practitioners such as naturopathic physicians or chiropractors may complete additional training to practice Ayurvedic methods.

Benefits and Risks of Ayurveda

Ayurveda represents a lifestyle orientation to health and health care. All aspects of an individual's life and circumstances influence health and illness, and Ayurvedic therapies target bringing all back into balance. Some herbal remedies may interact with other substances including prescription medications. A conventional doctor should provide clinical oversight for people who have health conditions that require conventional treatment, such as DIABETES, CANCER, and CARDIOVASCULAR DISEASE (CVD).

See also MEDICINAL HERBS AND BOTANICALS; NATIVE AMERICAN HEALING; TRADITIONAL CHINESE MEDICINE (TCM).

B

bilberry A plant (*Vaccinium myrtillus*) whose berries, stems, and leaves are rich in antioxidants (notably anthocyanosides) and tannins. Even preserves made from the blue-colored berries of this bush contain high enough levels of these substances to have noticeable effect. Anthocyanosides have particular affinity for the walls of arteries, especially arterioles, the tiny, almost microscopic arteries deep within body tissues where nutrient/waste exchanges takes place. Anthocyanosides appear to keep the cells of these arterial walls healthy and structurally intact. This action has pronounced effects on the tiny blood vessels that supply the RETINA, CORNEA, and other structures of the EYE, protecting them from age-related damage such as AGE-RELATED MACULAR DEGENERATION (ARMD) and CATARACT. The tannins in bilberry seem to help INFLAMMATION and INFECTION affecting the MOUTH and THROAT, plus gastrointestinal upset.

Many ophthalmologists recommend that people over age 50, who are entering the high-risk period of life for conditions such as ARMD, night blindness, and cataracts, take bilberry to help protect their eyes and vision. Bilberry seems most effective in combination with the amino acids LUTEIN and ZEAXANTHIN, which also protect the retina and cornea. There are no known side effects or interactions with bilberry, and doctors consider it safe for most people to take long-term.

BILBERRY *(Vaccinium myrtillus)*

Uses	Risks/Side Effects	Interactions
improve night vision prevent or slow ARMD prevent or slow growth of cataracts RETINOPATHY of DIABETES	none known	none known

See also ARTERY; CATARACT EXTRACTION AND LENS REPLACEMENT; RETINOPATHY; VISION IMPAIRMENT.

biofeedback A method in which a person learns to influence certain body responses, such as to PAIN or stress. Biofeedback begins with learning sessions that use electronic measuring devices to report physiologic signs such as PULSE, BREATHING rate, or SKIN temperature. The device sends a visual or sound signal to help focus concentration on the particular sign, for example the pulse. The person then concentrates on slowing the rate of the sound or visual cue, indicating that the body is relaxing and the HEART RATE is slowing. Over the course of 5 to 10 biofeedback sessions, the person learns to "tune in" to the physiologic signs and no longer needs the device. Once the person masters the method of biofeedback, he or she can use it at will.

CONDITIONS BIOFEEDBACK MAY HELP

ASTHMA	chronic PAIN syndromes
HYPERTENSION	migraine HEADACHE
MUSCLE tension headache	PALPITATIONS
RAYNAUD'S SYNDROME	RETINOPATHY of DIABETES
SEIZURE DISORDERS	stress
STROKE recovery	URINARY INCONTINENCE

Though the most common application of biofeedback is stress relief, people who have chronic health conditions also can use it to manage pain and other symptoms. Numerous clinical studies over the past 25 years have supported the effectiveness of biofeedback, especially for relieving pain and stress. There are few risks with biofeedback, as it is noninvasive. Because biofeedback can alter body chemistry, it can change medication needs for chronic conditions such as

DIABETES (INSULIN or oral ANTIDIABETES MEDICATIONS) and HYPERTENSION (high BLOOD PRESSURE).

See also HYPNOSIS; MEDITATION; MIND–BODY INTERACTIONS; STRESS AND STRESS MANAGEMENT; VISUALIZATION.

black cohosh An herbal remedy women may take to treat HOT FLASHES at MENOPAUSE. The medicinal extract comes from the dark roots and rhizomes of the wildflower black cohosh (*Actaea racemosa* or *Cimicifuga racemosa*), a member of the buttercup family indigenous to North America. Medicinal uses of black cohosh derive from NATIVE AMERICAN HEALING traditions. In 2001 the American College of Obstetricians and Gynecologists (ACOG) issued a statement of support endorsing black cohosh as a short-term treatment (up to six months) for relief of menopausal discomforts. Sold without a doctor's prescription as a dietary supplement in the United States, black cohosh is an ingredient in numerous women's health products.

The apparent active ingredients of black cohosh are deoxyactein, triterpenes glycosides (also called triterpenes saponins), and fukinolic acid, phytoestrogenic chemicals that produce a weak estrogen effect in the human body. Clinical studies of black cohosh generally support its effectiveness for relieving hot flashes, though results for other menopausal discomforts are less consistent. Studies also have failed to demonstrate any benefit for OSTEOPOROSIS.

As hot flashes are the major symptom for about 80 percent of women who have discomfort when going through menopause, many gynecologists recommend an initial trial of black cohosh in lieu of conventional estrogen/progesterone or estrogen hormone replacement therapy (HRT) for menopause. Many women find that a combination of botanicals in addition to black cohosh (such as flaxseed, soy, and chasteberry) seems to more effectively relieve symptoms, though these clinical research studies so far have not generated supportive evidence. Black cohosh does not seem very effective for menstrual discomforts such as cramps and excessive flow, though women have used it as a premenstrual/ menstrual remedy for several centuries. It typically takes 8 to 10 weeks to experience benefits after starting black cohosh.

Herbalists recommend black cohosh products that contain freeze-dried root, which appears to have the most potent and consistent action. Women who are pregnant should not take black cohosh because its estrogen-like actions may interfere with the body's hormonal balance. Some women experience gastrointestinal upset or dizziness; reducing the DOSE and taking the remedy with meals can minimize these side effects. Women who are taking oral contraceptives (birth control pills) should check with their doctors or pharmacists about possible interactions.

BLACK COHOSH ***(Actaea racemosa, Cimicifuga racemosa)***

Uses	Risks/Side Effects	Interactions
relieve menopausal HOT FLASHES	uterine contractions in PREGNANCY	oral contraceptives

See also DONG QUAI; GINSENG; PHYTOESTROGENS; SOY.

boswellia Medicinal preparations that derive from the resin of the *Boswellia serrata* tree native to the desert areas of India. Boswellia has strong anti-inflammatory characteristics and provides relief from OSTEOARTHRITIS and RHEUMATOID ARTHRITIS. It also provides relief from symptoms of INFLAMMATORY BOWEL DISEASE (IBD), especially in people who have Crohn's disease. In the United States boswellia is a dietary supplement available without a doctor's prescription. The typical course of treatment with oral forms of boswellia is 8 to 12 weeks. People who are taking prescription medications should check with their doctors before taking boswellia, though there are no known interactions between boswellia and other substances.

BOSWELLIA

Uses	Risks/Side Effects	Interactions
OSTEOARTHRITIS RHEUMATOID ARTHRITIS INFLAMMATORY BOWEL DISEASE (IBD)	none known	none known

See also NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS).

C

chamomile An herb, *Matricaria recutita,* used for its abilities to calm anxiety, soothe gastrointestinal irritation, relieve menstrual cramps, and aid in sleep. Chamomile contains volatile acids and flavonoids, chemical substances that ease spasms of smooth muscles, such as in the intestinal tract and the UTERUS, and that have mild anti-inflammatory qualities. The most active of these is the flavonoid apigenin, which has antiseptic properties as well.

Chamomile tea is a common preparation for stress relief and relaxation. In oral forms chamomile is a dietary supplement in the United States, available without a doctor's prescription. Topical forms of chamomile, also available over-the-counter, relieve itching and other SKIN discomforts, including those of dermatitis, and mild to moderate SUNBURN. Some preparations of chamomile dissolve or mix in bath water, such as powders and oils, providing full body relief.

Though there are few clinical studies that affirm the effects of chamomile, health experts consider it a generally safe medicinal herb. There are no known interactions or side effects. People who have allergies to ragweed, daisies, chrysanthemums, and other plants in the *Aster* family may have cross-over sensitivity to chamomile.

CHAMOMILE *(Matricaria recutita)*

Uses	Risks/Side Effects	Interactions
gastrointestinal upset sleep aid general relaxant	none known	none known

See also VALERIAN.

chelation therapy The therapeutic process of injecting or otherwise introducing a chemical agent, typically ethylenediaminetetraacetic acid (EDTA), into the body that binds with specific substances. The body then excretes the bound substances in the urine, safely eliminating them from the body. Doctors first used chelation therapy in the 1940s to treat poisoning with lead and other heavy metals, and that remains chelation therapy's accepted application in conventional medicine today.

Many of the first people to undergo chelation therapy were middle-aged men who had worked all their adult lives in factories where lead contamination was common. They also had the usual health conditions for men of their age, typically CARDIOVASCULAR DISEASE (CVD). As they completed the chelation therapy, many of the men also noticed they no longer had ANGINA PECTORIS (cardiac CHEST PAIN). The doctors conducting the chelation therapy treatments concluded the EDTA was also drawing calcium and other minerals from the ATHEROSCLEROTIC PLAQUE lining the CORONARY ARTERIES. The plaque narrowed the passageway for blood, causing the men to experience pain and shortness of breath particularly with exertion—the classic symptoms of CORONARY ARTERY DISEASE (CAD).

Though further testing and X-ray fluoroscopy of the men who experienced cardiovascular improvement failed to substantiate the theory, it has remained popular. However, there still are no clinical studies that support it. Another theory holds that chelation therapy removes from the body free radicals, particles of molecular waste that bind with any available molecule. This theory also remains unproven. Researchers believe free radicals that bind prevent bonded molecules from performing their intended functions, a process that over time results in degenerative diseases.

Though doctors in other countries may use chelation therapy before turning to surgical interventions to treat CAD, most conventional physicians in the United States feel the risks outweigh the benefits when it comes to chelation therapy as a treatment for atherosclerotic heart disease.

See also CORONARY ARTERY BYPASS GRAFT; HEAVY METAL POISONING; KIDNEY; LIFESTYLE AND CARDIOVASCULAR HEALTH; LIFESTYLE AND HEALTH.

Chinese herbal remedies See TRADITIONAL CHINESE MEDICINE (TCM).

chiropractic A system of health care that emphasizes manipulation of the spine and back to align the musculoskeletal system for optimal function and support of the rest of the body. Chiropractic originated in the United States with the work of Daniel David Palmer in the late 1890s. Palmer had a keen interest in magnetic HEALING and in what he perceived to be the body's natural tendency to keep itself in balance and thus in health. From his observations he began head and neck manipulations.

Chiropractic Diagnosis and Treatment

Chiropractic views the body as a system of balance, physical as well as emotional. When the spine is out of alignment, the rest of the body attempts to rebalance itself. When it cannot, one result is PAIN. Injuries and chronic health conditions may pull the spine out of alignment as well. The leading reason people seek chiropractic care is for treatment of musculoskeletal injuries and pain, particularly lower back pain. Chiropractic often is an effective approach for treating repetitious motion injuries as well as for teaching methods to avoid further injury. Chiropractic may incorporate ACUPUNCTURE, MASSAGE THERAPY, NUTRITIONAL THERAPY, or CRANIOSACRAL MASSAGE in addition to chiropractic manipulations.

The chiropractor begins an examination by asking questions about why the person has come for care and may take X-rays as well as look at the back. Observing posture and movement help the chiropractor assess overall musculoskeletal health, and the chiropractor will palpate the neck and spine. Most chiropractors also ask about diet and nutrition, physical activity and exercise, and occupation and recreational interests. The chiropractor should then explain his or her findings and the treatment options to correct them.

Chiropractic manipulations should not cause pain. Often the back makes popping sounds as the chiropractor uses pressure to correct subluxations (out of position vertebrae). Some chiropractors use devices, whereas others use only their hands. Most people feel relaxed after a chiropractic treatment. Chiropractic manipulation may correct one set of problems, which then reveals other problems. Some conditions require only a few visits and treatments, though others may require up to 10 visits over several weeks or occasionally more extensive therapy. No chiropractic therapy should continue indefinitely, though many people need to return periodically.

Chiropractic manipulation can restore the spine's correct alignment, but circumstances such as structural asymmetries, longstanding injury, and postural or function-oriented habits that remain unchanged may cause the spine to eventually return to misalignments. Many people have one leg slightly different length from the other, for example, or may sit at a computer all day leaning forward with shoulders hunched. These chronic sorts of circumstances account for about a third of chiropractic visits.

Chiropractic Practitioners

Over the decades since Palmer introduced his methods for manipulating the neck, chiropractic has evolved into a comprehensive and structured health-care discipline. Doctors of chiropractic (DCs) attend eight or more years of college and chiropractic medical school, completing extensive education and training in a broad spectrum of health-care areas. Many chiropractors have further training, certification, or licensure in acupuncture, nutrition, and specialized care such as sports injuries. All states in the United States require chiropractors to pass a national proficiency examination and meet the state's licensing requirements.

Benefits and Risks of Chiropractic

At one time in its evolution, chiropractic involved approaches and methods, arising from inconsistencies in practice and education, that sometimes did harm to people. Standardizations in philoso-

phy, education, and licensing in the latter half of the twentieth century solidified chiropractic as a beneficial, reputable health-care profession and practice. In 1994 the US Agency for Health Care Policy and Research (AHCPR) endorsed chiropractic as a safe and appropriate first-line treatment for low back pain. Most insurers in the United States pay for limited chiropractic care.

Chiropractors may not prescribe medications, diagnose health conditions, provide medical treatments outside those necessary for spinal manipulations, or perform surgery. People who have health conditions that affect the spine such as ANKYLOSING SPONDYLITIS or RHEUMATOID ARTHRITIS should talk with their orthopedists before undergoing chiropractic treatment. A conventional doctor should evaluate back pain with FEVER, as this may be an indication of MENINGITIS or other potentially life-threatening infection.

See also NATUROPATHY; OSTEOPATHIC MANIPULATIVE TREATMENT (OMT).

chondroitin A chemical compound that occurs naturally in the CARTILAGE and other tissues in the joints, chondroitin appears to protect JOINT tissues from damage and deterioration by blocking the actions of certain destructive enzymes. There is substantial evidence, through clinical studies, that this blocking action can arrest and even reverse OSTEOARTHRITIS. In some studies, chondroitin was at least as effective as the commonly prescribed NONSTERIODAL ANTI-INFLAMMATORY DRUGS (NSAIDS) that are the standard treatment for osteoarthritis in the United States. Combining chondroitin with another natural compound, GLUCOSAMINE, intensifies the benefit.

Though researchers and practitioners have known of glucosamine and have recommended it to relieve joint INFLAMMATION and PAIN for decades, researchers discovered chondroitin only in the 1960s. A number of clinical studies conducted in the 1980s and 1990s began to make clear chondroitin's effects and benefits. Chondroitin seems most effective for osteoarthritis affecting the hips and knees and does not have any effect on RHEUMATOID ARTHRITIS, a deformative autoimmune disorder.

There seem to be few side effects or interactions with chondroitin. People who are taking anticoagulant medications should check with their doctors before taking chondroitin. Though chondroitin does not directly affect clotting, many substances that affect inflammation have the potential for interfering with blood chemistry. It typically takes two to four months to notice appreciable results after starting chondroitin.

CHONDROITIN

Uses	Risks/Side Effects	Interactions
OSTEOARTHRITIS	none known	possibly anticoagulants

See also ANTICOAGULANT THERAPY; AUTOIMMUNE DISORDERS; SAMe.

coenzyme Q10 An ANTIOXIDANT found in every nucleated cell in the body. It has numerous functions related to cell activity and repair. As a coenzyme, coenzyme Q10 facilitates or works in collaboration with enzymes in the cells. Enzymes carry out the genetic instructions of the cell. The more active the cell, the more coenzyme Q10 the cell contains. A HEART cell has considerably more coenzyme Q10 than does a SKIN cell, for example. Researchers discovered coenzyme Q10 in 1957 and continue to investigate how it works and what it does in the body.

People who have certain forms of heart disease, such as HYPERTENSION (high BLOOD PRESSURE) and HEART FAILURE, have lower than normal levels of coenzyme Q10. In some studies, giving them coenzyme Q10 improved heart function, most notably hypertension. Though researchers do not fully understand its mechanisms, boosting coenzyme Q10 levels in cardiac cells seems to improve their efficiency. This effect is less conclusive in people recovering from HEART ATTACK or who have other forms of heart disease.

There is some evidence that coenzyme Q10 supplementation has numerous beneficial effects on health. Researchers are exploring its role in preventing BREAST CANCER, periodontitis (INFLAMMATION and INFECTION of the gums), and ALZHEIMER'S DISEASE. Some health experts believe coenzyme Q10 may improve symptoms and QUALITY OF LIFE for people with MITOCHONDRIAL DISORDERS, MUSCULAR DYSTROPHY, and degenerative neurologic conditions such as PARKINSON'S DISEASE. Studies investigating the ability of coenzyme Q10

supplementation to prevent the onset of type 2 DIABETES have so far yielded no evidence that it can do so. Nor is there any conclusive evidence that coenzyme Q10 has any ability to enhance IMMUNE SYSTEM function, though all of these effects have theoretical potential. Across the spectrum of health knowledge, coenzyme Q10 is a relatively new discovery and much remains for researchers and doctors to learn and understand about its natural functions in the body as well as the benefits and possible risks of supplements.

Coenzyme Q10 is available in the United States as a dietary supplement that does not require a doctor's prescription to obtain. It does not appear to have side effects or interactions with other substances, though health experts encourage people to talk with their doctors about taking it if they are taking medications to treat health conditions, especially hypertension and heart failure. Pregnant or BREASTFEEDING mothers probably should not take coenzyme Q10 as researchers know little about how it might affect infants. Coenzyme Q10 is fat soluble; the body best absorbs it with foods that contain some dietary fat.

COENZYME Q10

uses	Risks/Side Effects	Interactions
HYPERTENSION HEART FAILURE recovery after HEART ATTACK periodontitis	none known	none known

See also LIFESTYLE AND CARDIOVASCULAR HEALTH; PERIODONTAL DISEASE.

craniosacral massage A form of bodywork, also called craniosacral therapy, in which the practitioner gently manipulates the head, neck, and spine to balance the fluids around the head and SPINAL CORD. The movement of this fluid, in the context of craniosacral massage, is the cranial rhythmic impulse. The intended goal is somatoemotional release, the discharge of physical and emotional tension the head and spine hold as a result of stress and daily experiences. Injuries may also contribute to the tension.

For many people the experience evokes the sensation of floating or dreaming and is profoundly relaxing. Though the craniosacral therapist's movements are gentle and touch is very light, there is a sensation of movement throughout the body. Sometimes the craniosacral therapist will also manipulate the spine, though also very gently and not at all in the way a chiropractor performs spinal manipulation.

A craniosacral therapist is usually trained and licensed (in compliance with relevant state requirements) as a massage therapist or physical therapist, though some naturopathic physicians, chiropractors, and osteopathic physicians also have training in craniosacral techniques. As with all touch therapy, it is important to feel comfortable with, and trust, the practitioner. The manipulations of the body release stored physical and emotional energy that can result in unexpected surges of feelings and even discomfort. But nearly everyone feels deeply relaxed following a craniosacral massage.

See also CHIROPRACTIC; MASSAGE THERAPY; MIND–BODY INTERACTIONS; PHYSICAL THERAPY.

D–F

dehydroepiandrosterone (DHEA) A steroid HORMONE that occurs naturally in the body. It serves as a precursor primarily to estrogen in women and TESTOSTERONE in men, though women also convert small amounts to testosterone and men convert small amounts to estrogen. Levels of endogenous DHEA gradually diminish with aging. As a supplement, DHEA provides a similar source to the body for these hormones. DHEA is available without a doctor's prescription in the United States, marketed as a dietary supplement sold mostly in health food stores.

People take DHEA supplement for numerous and diverse uses such as to increase libido, reduce the effects of aging, boost immune function, prevent OSTEOPOROSIS, relieve symptoms associated with FIBROMYALGIA and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), and prevent degenerative diseases related to aging such as CARDIOVASCULAR DISEASE (CVD). There is scant clinical evidence to support any of these uses, and doctors worry that increasing the body's levels of sex hormones may increase the risk for hormone-driven BREAST CANCER and PROSTATE CANCER. There is some evidence that long-term DHEA use damages the LIVER.

Though DHEA is an over-the-counter dietary supplement in the United States, doctors encourage people to obtain blood tests to measure their levels of estrogen or testosterone before taking DHEA. The greatest risk for adverse health circumstances occurs when products such as DHEA increase estrogen or testosterone blood levels to higher than normal. Researchers believe this make increase the risk for some cancers, although again clinical evidence is lacking. Health experts recommend that people under age 50 do not take DHEA unless a doctor prescribes it to treat conditions in which endogenous DHEA levels are low.

DEHYDROEPIANDROSTERONE (DHEA)

Uses	Risks/Side Effects	Interactions
FIBROMYALGIA	acne flareups	none known
SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)	mood swings	
mental alertness in aging	LIVER damage	
slow OSTEOPOROSIS		

See also ADRENAL INSUFFICIENCY; ANABOLIC STEROIDS AND STEROID PRECURSORS; HUMAN GROWTH HORMONE (HGH) SUPPLEMENT; MELATONIN.

dong quai An ancient remedy for relieving menstrual and menopausal discomforts. It contains phytoestrogens, which are estrogen-like chemicals that are much weaker than those the human body produces though are nonetheless capable of binding with estrogen receptors. Researchers do not know the extent to which dong quai's phytoestrogens have any effect in the body, however, because dong quai contains other active ingredients and often appears in combination with other herbs. Dong quai (*Angelica sinensis*) also contains coumarins, chemicals that cause smooth MUSCLE tissue to relax. This effect dilates blood vessels, increasing blood flow. It also acts to relax the UTERUS, which is also smooth muscle tissue. Many health experts believe coumarins are responsible for most of dong quai's effects. Dong quai is sold as an over-the-counter dietary supplement in the United States.

Dong quai also contains psoralens, chemicals that interact in the SKIN when exposed to sunlight. Psoralens intensify the effects of ultraviolet light with the result of unusually rapid and severe SUNBURN. Women should limit sun exposure when taking dong quai. Dong quai also may interact

with NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), causing stomach upset, irritation, and bleeding. Because dong quai affects blood flow, it may also alter the intended effects of anticoagulant medications. And because of its actions to relax smooth muscle including the UTERUS, women should not take dong quai when they are pregnant.

DONG QUAI *(Angelica sinensis)*

Uses	Risks/Side Effects	Interactions
menstrual cramps	excessive bleeding	anticoagulants
menopausal discomforts	stomach irritation	NSAIDs
ENDOMETRIOSIS		

See also BLACK COHOSH; DYSMENORRHEA; MENOPAUSE; MENSTRUATION; PREMENSTRUAL SYNDROME; SOY.

echinacea An herb with immune-supportive properties. Echinacea remedies incorporate stems, leaves, and seeds or their extracts from three of the nine species of echinacea (*Echinacea angustifolia, E. pallida, E. purpurea*). Though herbalists typically use certain of the species according to the desired immune effect, commercially produced echinacea products typically contain a mix. The most common use of echinacea is to lessen the severity of COLDS, INFLUENZA, and other upper respiratory infections. Echinacea seems most effective when taken at the first indication of symptoms and can shorten the length of illness by 20 to 60 percent.

Echinacea seems less effective in protecting against upper respiratory infections when taken as a general prophylactic measure, though regular use may prevent canker sores. Health experts caution people to take echinacea for no longer than three weeks to give their immune systems a break from the echinacea's stimulation and to wait one week before taking another course of echinacea. Some herbalists recommend using echinacea in rotation with other immune-boosting herbs. There is no clinical evidence to support a role for echinacea in preventing infections such as HIV/AIDS or HEPATITIS. Though echinacea may additionally support the IMMUNE SYSTEM when taken in conjunction with ANTIBIOTIC MEDICATIONS to treat bacterial infections, it cannot replace antibiotics.

Some studies have shown echinacea to have adverse effects in people who are IMMUNOCOMPROMISED, although this finding has been inconsistent. Doctors generally recommend against echinacea for people who have chronic immune system disorders such as RHEUMATOID ARTHRITIS, MULTIPLE SCLEROSIS, and SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), because echinacea can overstimulate the immune system and make symptoms worse. Some people who have CHRONIC FATIGUE SYNDROME have experienced improvement with echinacea and other immune-enhancing herbs, however. People who have immune system disorders should discuss echinacea with their regular doctors before taking echinacea. Echinacea is available as a dietary supplement in the United States. People who are allergic to plants in the daisy (*Aster*) family may also be allergic to echinacea.

ECHINACEA *(E. angustifolia, E. pallida, E. purpurea)*

Uses	Risks/Side Effects	Interactions
prevent COLDS and INFLUENZAnone	none known	none known
reduce cold/flu duration		
general IMMUNE SYSTEM support		

See also CANKER SORE; GOLDENSEAL; INFECTION.

feverfew An herb once popular for, as its name implies, lowering FEVER. However, current use focuses on its ability to prevent migraine headaches from developing and to minimize the symptoms of migraines when they do occur. The primary active ingredients researchers have isolated in feverfew (*Tanacetum parthenium*) are parthenolides, a group of mild prostaglandin suppressants. PROSTAGLANDINS are chemicals the body releases that are associated with PAIN. Aspirin and other NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) achieve much of their pain-relieving effects through prostaglandin suppression. Prostaglandins also are factors in the inflammatory processes associated with fever.

The form of feverfew that appears most effective in preventing migraine headaches is the freeze-dried herb. However, the level of parthenolides in feverfew plants varies widely. Capsules and tablets appear to have little or no effect for

migraines, though may provide a level of relief for menstrual discomforts. Results become evident after taking feverfew for eight weeks or longer. Feverfew inhibits PLATELET AGGREGATION, slowing the initiation of COAGULATION (the formation of blood clots). People who take feverfew should let their surgeons know of this, if they are planning surgery, and stop taking the herb for the time period the surgeon recommends. People should not take feverfew with prescribed anticoagulant medications such as warfarin or enoxaparin.

FEVERFEW *(Tanacetum parthenium)*

Uses	Risks/Side Effects	Interactions
migraine HEADACHE	excessive bleeding	anticoagulants
menstrual discomfort		aspirin, NSAIDs

See also ANALGESIC MEDICATIONS; BIOFEEDBACK; BIOFEEDBACK AND PAIN RELIEF.

flower essences Remedies that capture the energy and HEALING qualities of plants and flowers and impart them to alter emotional responses that might be causing physical disease. The most widely use flower essence formulas are the Bach flower essences, named for the Dr. Edward Bach, who developed and popularized flower essence therapy in the 1930s. Bach, a homeopathic physician, observed the correlations between emotion and physical illness. He surmised that plants and flowers could alter emotional responses, freeing the body to return to a state of health. In the tradition of HOMEOPATHY, Bach created mixtures that started with parts of plants in solutions of water and ALCOHOL. He repeatedly diluted the solutions until virtually no plant particle remained. The residual solution retained the energy of the flower, however, which could influence the emotions of people who used the solution.

No clinical studies support the effectiveness of flower essences, though people who use them typically report improvement in their symptoms. From the homeopathic perspective the flower essences influence health in the fashion of "like cures like," the underlying philosophy of homeopathy. From the conventional medicine perspective, flower essences may improve the emotional well-being of people who take them through the PLACEBO effect. Most health experts agree that with remedies, such as flower essences, that have no potential side effects, there is no harm in using the remedies. It is important to remember, however, that some emotional states may reflect potentially serious conditions such as GENERALIZED ANXIETY DISORDER (GAD) and DEPRESSION. There are conventional medicine therapies for these conditions that are likely to provide more rapid and effective intervention. Flower essences are widely used in an integrative manner in many European countries.

See also ANTIANXIETY MEDICATIONS; ANTIDEPRESSANT MEDICATIONS; AROMATHERAPY.

garlic In ancient times people used garlic to ward off the evil vapors and spirits they believed responsible for illness. In modern times doctors know more about what really causes many of the health circumstances that result in disease. People use garlic and garlic supplements to improve BLOOD circulation, lower BLOOD PRESSURE, and reduce blood cholesterol, the key factors that contribute to CARDIOVASCULAR DISEASE (CVD). The active ingredients in garlic (*Allium sativum*) are allium compounds (also found in onions and leeks), sulfur-based substances that give garlic its distinctive odor and flavor as well as its medicinal benefits.

More than 100 clinical research studies point to allium compounds as the substances responsible for these benefits. Allium compounds contain two dozen or so chemicals that

- reduce PLATELET AGGREGATION, making it more difficult for the blood cells that initiate the clotting process to stick together
- help maintain the FLEXIBILITY of ARTERY walls
- may block cholesterol production in the LIVER, reducing the blood levels in particular of the low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterols associated with ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD)
- have mild anti-inflammatory effects, helping reduce irritation and INFLAMMATION of the inner walls of the arteries that researchers believe sets the stage for arterial plaque accumulations that form the basis of atherosclerosis and CAD
- have mild antibacterial effects that improve resistance to infections affecting the MOUTH and THROAT

These effects seem the same whether the source of the garlic is the natural bulb or supplements. Some studies show as much as a 6 to 10 milligram per deciliter (mg/dL) reduction in total blood cholesterol levels after taking garlic supplements for three months, about the same result doctors expect to see with lipid-lowering medication therapy. The combined effect of garlic's actions on the cardiovascular system help lower blood pressure by decreasing the resistance blood encounters as it flows through the arteries. Though the preventive benefit for HEART ATTACK and STROKE is difficult to measure, many health experts agree that the many effects of garlic, however small, add up to reduced risk for cardiovascular disease, especially in combination with other lifestyle factors such as regular daily exercise, weight loss, and SMOKING CESSATION. Some health experts believe garlic and garlic supplements also lower the risk for DIABETES type 2 by improving INSULIN sensitivity, though clinical studies so far have failed to bear this out. Nor is there much evidence supporting garlic's ability to reduce CANCER risk.

Garlic and garlic supplements are relatively safe for most people to take, though may intensify the effect of many common antihypertensive medications. People who are taking medications to treat high blood pressure should first talk with their doctors before beginning a garlic regimen. The amounts of garlic a person might use in seasoning foods are not enough to cause this interference, though the amounts of garlic in therapeutic products can interact with numerous medications. Because garlic affects clotting, surgeons generally request people stop taking it before any scheduled operations.

GARLIC *(Allium sativum)*

Uses	Risks/Side Effects	Interactions
lower blood cholesterol lower risk for ATHEROSCLEROSIS reduce BLOOD PRESSURE	gastrointestinal upset strong body and breath odor excessive bleeding with surgery	antihypertensives

See also ANTICOAGULATION THERAPY; COAGULATION; INFECTION; LIFESTYLE AND CARDIOVASCULAR HEALTH.

ginger An herb that soothes gastrointestinal upset. More likely to be in the kitchen spice cabinet than the medicine cabinet, ginger (*Zingiber officinale*) is one of the most popular spices. Herbalists and cooks alike use the gnarly root fresh or dried, sliced or powdered, in natural form or prepared as an extract. TRADITIONAL CHINESE MEDICINE (TCM) considers ginger a hot, yang energy that brings warmth to the HEART, LUNGS, and especially the STOMACH to improve their functions. Folk medicine advises pregnant women to suck on thin slices of fresh gingerroot to alleviate symptoms of MORNING SICKNESS. A popular home remedy for stomach upset is sipping on a flat gingerale. Ginger also contains substances that act as mild antihistamines, helping relieve allergy symptoms such as ALLERGIC RHINITIS.

Clinical research studies provide supporting evidence of ginger's abilities to relieve

- NAUSEA, particularly that related to PREGNANCY (morning sickness), motion sickness, and CHEMOTHERAPY
- nausea and VOMITING due to gastrointestinal viruses
- dizziness related to motion sickness
- digestive upset, particularly FLATULENCE (intestinal gas)
- congestion due to COLDS, INFLUENZA, and seasonal allergies

Though some people experience mild gastric irritation when taking ginger supplements or drinking ginger tea, ginger causes very few side effects and health experts consider it safe for nearly everyone to take. Ginger may affect PLATELET AGGREGATION, and thus BLOOD clotting (COAGULATION), in some people so surgeons generally ask people to stop taking ginger a few days before any planned surgery.

GINGER *(Zingiber officinale)*

Uses	Risks/Side Effects	Interactions
general NAUSEA MORNING SICKNESS motion sickness nausea of CHEMOTHERAPY digestive upset	excessive bleeding	anticoagulants ASPIRIN THERAPY

See also ANTIEMETIC MEDICATIONS; ANTIHISTAMINE MEDICATIONS; HISTAMINE.

ginkgo biloba An herbal product with many uses. The ginkgo biloba tree is the oldest living species of tree on Earth, believed to have first appeared more than 200 million years ago in the area that is now China. Individual trees typically live hundreds of years, with some documented to be nearly 1,000 years old, and now grow in many parts of the world. Herbal remedies made from the leaves and seeds of this ancient tree have been popular for centuries for increasing longevity and improving mental focus. It contains numerous antioxidants (notably quercetin), collectively identified as ginkgo biloba extract (GBE) on supplement product labels. In the United States ginkgo biloba is a dietary supplement available without a doctor's prescription.

Clinical research studies conducted in the 1990s and early 2000s demonstrated ginkgo's ability to improve BLOOD circulation in the BRAIN and the smallest of arteries, the arterioles, throughout the body. Studies among people with ALZHEIMER'S DISEASE and other forms of DEMENTIA (diminished thought capacity and memory) showed significant improvement after taking ginkgo biloba supplements for eight weeks or longer, especially in combination with *Panax* GINSENG. Many people of all ages who take ginkgo biloba do so for these cerebrovascular benefits. The effect seems to arise from ginkgo's mild anticoagulant action in combination with its ANTIOXIDANT activity. Ginkgo's ability to open up peripheral circulation also improves conditions such as PERIPHERAL VASCULAR DISEASE (PVD), NEUROPATHY of DIABETES, and ERECTILE DYS-

FUNCTION related to ATHEROSCLEROSIS (as is most erectile dysfunction in men age 60 and older). There is also likely a preventive effect against embolytic STROKE and HEART ATTACK.

For most people, health experts consider ginkgo biloba safe at recommended doses. Because ginkgo biloba affects blood clotting, people who are having surgery should let their surgeons and anesthesiologists know they are taking it. The doctor may ask the person to stop taking the supplement for a week or two before the surgery and for a period of time after the surgery, until HEALING is adequate to end the risk for postoperative bleeding. People who take ANTICOAGULANT THERAPY (including ASPIRIN THERAPY) should talk with their doctors before taking ginkgo, as it may intensify the anticlotting effect. Gingko biloba also affects INSULIN production and sensitivity, which may improve prediabetes and noninsulin-dependent type 2 diabetes though can interfere with ANTIDIABETES MEDICATIONS and INSULIN THERAPY in people who have insulin-dependent diabetes (type 1 or type 2).

GINKGO BILOBA

Uses	Risks/Side Effects	Interactions
RAYNAUD'S SYNDROME	excessive bleeding	anticoagulants
INTERMITTENT CLAUDICATION	elevated BLOOD PRESSURE	antihypertensives
PERIPHERAL VASCULAR DISEASE (PVD)		thiazide diuretics
ATHEROSCLEROSIS		trazodone
CORONARY ARTERY DISEASE (CAD)		prochlorperazine
ALZHEIMER'S DISEASE		ASPIRIN THERAPY

See also ANTI-AGING APPROACHES; ARTERY; INSULIN RESISTANCE; LIFESTYLE AND HEALTH.

ginseng A botanical product prepared from the root of the ginseng plant. There are two major varieties of ginseng, Asian ginseng (*Panax ginseng*) and American ginseng (*Panax quinquefolius*). As well, there are dozens of subvarieties within each. Asian ginseng, also called Chinese or Korean ginseng, is indigenous to the Asian continent. American ginseng, also called North American ginseng, grows naturally on the North American continent. The designation "*Panax* ginseng" refers to the major varieties and their subvarieties collectively; "*Panax ginseng*" with both words italicized refers to Asian ginseng. The herb commonly called Siberian ginseng (*Eleutherococcus senticosus* or *Acanthopanax senticosus*) is not true ginseng but rather a "look-alike" botanical cousin that has a different chemical composition and different effects as an herbal remedy. Ginseng is sold as a dietary supplement in the United States and available in various forms without a doctor's prescription.

Panax Ginseng

The varieties of *Panax* ginseng include differing amounts of three major kinds of chemicals

- ginsenosides, which function as mild stimulants to sharpen mental focus and possibly improve cognitive function and memory
- panaxans, which may improve INSULIN sensitivity
- polysaccharides, complex sugar molecules that aid IMMUNE SYSTEM functions

***PANAX* GINSENG**

Uses	Risks/Side Effects	Interactions
mental clarity and focus	insomnia	loop diuretics
memory improvement	excitability	CAFFEINE
IMMUNE SYSTEM support		
aphrodisiac		
INSULIN RESISTANCE		
type 2 DIABETES		

The color of ginseng, red or white, reflects the kind of processing method used in its preparation. Medicinal preparations use only the ginseng root. Red ginseng is steam processed, which preserves more of the natural ginsenosides. White ginseng is sun dried. Herbalists consider red ginseng more potent than white ginseng. Most people take ginseng for improved mental alertness, and for its IMMUNE RESPONSE properties. Ginseng also has gained popularity as an aphrodisiac, likely as a result of its mild STIMULANT effect. Some research studies support the claimed benefits of sharpened mental focus and improved cognitive function, especially when taken in combination with GINKGO

BILOBA, though any effects on LIBIDO beyond heightened alertness remain unclear. A number of energy drinks and similar products contain ginseng, though not in amounts likely to produce any effects.

Acanthopanax (Siberian Ginseng)

Herbalists call this ginseng cousin by the common name Acanthopanax. The plants of Acanthopanax look similar to true ginseng and are indigenous to northern China and the region of southern Russia once called Siberia, hence the misnomer Siberian ginseng. However, Acanthopanax contains eleutherosides, which have strong STIMULANT characteristics, rather than ginsenosides. Both eleutherosides and ginsenosides belong to the same chemical family, saponins, which have a range of actions including CENTRAL NERVOUS SYSTEM stimulation, antibiotic properties, and immune response. Asparagus root, onion, and GARLIC also contain saponins. The stimulant effect of Acanthopanax is strong enough that this ginseng relative is on the list of banned substances for Olympic athletes. Herbalists value Acanthopanax as a tonic (preparation that increases STRENGTH and ENDURANCE) rather than a medicinal herb.

People who have HYPERTENSION (high BLOOD PRESSURE) and women who are pregnant should not take Acanthopanax. Women should temporarily stop taking Acanthopanax during their menstrual periods as it may cause excessive bleeding. Most herbalists recommend taking Acanthopanax no longer than 90 days, then taking a three- to six-week break before taking it again.

***ACANTHOPANAX* GINSENG**

Uses	Risks/Side Effects	Interactions
alertness athletic enhancement	elevated BLOOD PRESSURE excitability, irritability insomnia excessive menstrual bleeding	antihypertensive medications furosemide (Lasix)

See also TRADITIONAL CHINESE MEDICINE (TCM).

glucosamine A GLUCOSE compound the body uses to produce the chemical substances it needs to repair and maintain JOINT CARTILAGE, ligaments, and tendons. In health, the body generates sufficient quantities of endogenous glucosamine through a complex series of metabolic interactions. When damage through wear and tear occurs to the joints, the body may have difficulty keeping pace with its glucosamine needs. The older the person, the more quickly the body reaches the point at which it cannot produce enough glucosamine to produce the substances to repair joint tissues. The result is OSTEOARTHRITIS—INFLAMMATION and degeneration of the cartilage and related tissues in the joint.

Doctors in Europe and numerous countries around the world prescribe glucosamine supplementation to replenish the body's supply and allow the natural HEALING processes to take place. Veterinarians in the United States similarly use glucosamine to treat osteoarthritis in domestic pets as well as large animals such as horses. However, doctors in the United States do not often consider glucosamine as a possible treatment for osteoarthritis, in part because NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), which became popular in the late 1970s and early 1980s, are so effective at controlling both the PAIN and the inflammation characteristic of osteoarthritis and in part because there were few clinical research studies to support glucosamine's effectiveness.

Clinical studies in the 1980s and 1990s began to show objective evidence that glucosamine supplements (exogenous glucosamine) seemed able to at least partially restore the body's ability to heal osteoarthritis damage, and some doctors started recommending it for people who could not tolerate the gastrointestinal irritation of NSAIDs. About half of the people in the studies experienced moderate to significant relieve from pain, stiffness, and limited range of motion in arthritic knees and hips. The effect seems even more profound when taking glucosamine in combination with CHONDROITIN, another glucose-based structure (called a complex polysaccharide).

However, researchers continue to debate whether glucosamine taken as a supplement has the same action in the body as endogenous glucosamine. So far clinical research studies have failed to reveal the actions of exogenous glucosamine once it enters the body. Because glu-

cosamine is a dietary supplement in the United States, it is available without a doctor's prescription, so people who have osteoarthritis can sidestep the controversy and take the substance if they choose. Glucosamine seems to have little effect on RHEUMATOID ARTHRITIS, an autoimmune disorder that not only destroys but also deforms the joints.

Glucosamine partially blocks the absorption of many diuretic medications such as furosemide (Lasix) and the thiazides. Though people can take both products at the same time, doctors may increase the diuretic DOSE for as long as the person is also taking glucosamine. Among the minor side effects are NAUSEA and gastrointestinal upset.

GLUCOSAMINE

Uses	Risks/Side Effects	Interactions
OSTEOARTHRITIS chronic BACK PAIN	gastrointestinal upset	loop diuretics

See also AUTOIMMUNE DISORDERS; LIGAMENT; SAMe; TENDON.

goldenseal An herb (*Hydrastis canadensis*) with anti-inflammatory and possibly anti-INFECTION properties. Indigenous to the North American continent (and in particular to the Pacific Northwest), goldenseal is a mainstay of NATIVE AMERICAN HEALING. Early tribes ground the roots into a mushy paste to use as a poultice to treat insect bites, LACERATIONS, and rashes. They also brewed the roots into tea, which though bitter to the taste was an effective remedy for digestive upset. Today products containing goldenseal extract come in topical, oral, and dried forms.

Researchers have isolated goldenseal's active ingredients as berberine and hydrastine, substances that now manufacturers extract and produce as prescription medications for use as in a number of European countries. Berberine in particular has strong antibiotic action and acts to stimulate IMMUNE RESPONSE in the body. Goldenseal taken in combination with ECHINACEA, another herb that boosts immune function, appears to increase resistance to many infections from COLDS and INFLUENZA to HEPATITIS.

Goldenseal is often an ingredient in herbal preparations to relieve the adverse effects of CHEMOTHERAPY and to support the IMMUNE SYSTEM in fighting the cancer. As with other immunosupportive therapies, health experts recommend using goldenseal for no longer than three weeks consecutively, with two to four weeks between treatments. This allows the immune system to rest and restore itself. There are no known side effects or interactions with goldenseal.

GOLDENSEAL *(Hydrastis canadensis)*

Uses	Risks/Side Effects	Interactions
topical and systemic antibioticnone stimulate IMMUNE RESPONSE soothe digestive upset calm and help heal canker sores increase resistance to urinary tract infections	none known	none known

See also CANKER SORE; GASTROENTERITIS; GREEN TEA; RASH; SAMe; URINARY TRACT INFECTION (UTI).

green tea The unfermented, dried leaves of the tea plant (*Camellia sinensis*), brewed into a drink. Black tea and green tea come from the same plant. The difference between them is that processing and drying of green tea leaves takes place immediately after harvesting them and black tea leaves undergo a processing that includes fermentation before drying. Though both kinds of tea leaves contain the same chemical compounds, green tea contains them in far greater concentrations. Green tea is also available in the United States as a dietary supplement, packaged in capsules or as tablets that contain the dried leaves ground into powder. Green tea contains a number of antioxidants, called polyphenol catechins. They include gallocatechin (GC), epigallocatechin (EGC), epicatechin (EC), and the especially potent epigallocatechin gallate (EGCG). Red grapes and red wine also contain high amounts of these catechins.

EGCG appears to interfere with enzyme processes necessary to allow healthy cells to mutate into cancerous cells, thus thwarting the development of CANCER. It also seems to initiate apoptosis, a sequence of natural events leading to cell death, in cancer cells that are already present. In addition to its cancer-fighting actions, EGCG

has the ability to kill certain BACTERIA including *Helicobacter pylori*, the bacteria responsible for much PEPTIC ULCER DISEASE, and *Escherichia coli*, the bacteria that causes serious GASTROENTERITIS. Researchers continue to study all of these actions to further understand how they occur and what they might bode for cancer prevention efforts.

The other catechins have ANTIOXIDANT actions that appear to help the body resist changes in the cells of the ARTERY walls that allow ATHEROSCLEROSIS to establish itself. Other ingredients in green tea include tannins, which act to soothe the mild to moderate digestive upset, and fluoride, which strengthens the TEETH. Green tea and green tea extract products naturally contain CAFFEINE. Green tea also contains theanine, a substance with anti-anxiety effects that somewhat counter the effect of the caffeine. Though there are no known health risks or interactions with green tea, people who ingest high quantities may experience sleep disturbances and irritability as a consequence of too much caffeine. Because of green tea's caffeine content, health experts recommend pregnant and nursing mothers limit consumption.

GREEN TEA *(Camellia sinensis)*

Uses	Risks/Side Effects	Interactions
prevent development of cancer prevent spread of cancer eliminate existing cancer cells soothe digestive upset decrease low-density lipoprotein cholesterol (LDL-C) improve circulation strengthen the TEETH fight bacterial MOUTH infections	excessive CAFFEINE consumption	none known

See also COENZYME Q10.

homeopathy A system of medicine based on the philosophy that symptoms represent the body's efforts to heal. Homeopathic treatment attempts to further stimulate those efforts through the premise that "like cures like," as homeopathy founder Samuel Hahnemann expressed it. Treatment employs homeopathic remedies that are extremely diluted solutions of substances such as herbs, plants, and minerals; some may contain chemicals and even toxins. In the United States, the US Food and Drug Administration (FDA) regulates homeopathic remedies. Manufacturers must comply with the standards and procedures of the *Homeopathic Pharmacopoeia of the United States*.

Homeopathic Diagnosis and Remedies

The homeopathic practitioner makes a diagnosis of symptoms rather than disease. He or she does so by listening to what the person describes and conducts an examination appropriate for the practitioner's scope of practice. The practitioner then prescribes homeopathic remedies that support the symptoms to help the body use those symptoms to rid itself of whatever ailment is present. The premise is that the body uses its own resources and energy to heal itself. There are more than 3,000 homeopathic remedies, each of which applies to a certain symptom or constitution. A person takes the remedies that apply to his or her circumstances, making homeopathic treatment entirely individualized.

The essential principle of homeopathic remedy preparation is that the vigorous shaking, called succession, that follows each step of dilution intensifies the potency of the solution by dispersing the energy of its molecules into the molecules of the water and ALCOHOL in the solution. Even when the solution has become so dilute that there are no detectable molecules of the original ingredient remaining, homeopathy asserts the remedy still holds the "molecular memory" of the active ingredient. The concentrations of homeopathic remedies reflect sequential dilutions. Mixing the solution with powdered lactose creates product forms other than liquids.

HOMEOPATHIC REMEDY DILUTIONS

Dilution	Sequential Ratios	Designation
decimal	1:10	C (1C, 2C, 3C, etc.)
centesimal	1:100	X (1X, 2X, 3X, etc.)
millesimal	1:1000	M (1M, 2M, 3M, etc.)

Homeopathic remedies carry the Latin names of their original ingredients, along with the designations for their dilutions. Many also include common names as well. The higher the dilution ratio, the more dilute the remedy. Homeopathic remedies come in tablets, granules, liquids, ointments, creams, and suppositories.

Homeopathic Practitioners

Homeopathy originated in Europe in the 1700s with the work of Samuel Hahnemann, a German chemist. Hahnemann embarked on a quest to find better ways to treat illness than the harsh and often damaging methods, such as bloodletting (the practice of bleeding a person who was ill to rid the body of toxins), popular at the time. His approach was, for its time, highly scientific and the mildness of homeopathic remedies quickly acquired a loyal following. A Boston physician, Hans Burch Gram, studied homeopathy in Europe and opened a homeopathic practice when he returned to the United States in 1825. The philosophy gained popularity over the ensuing decades, peaking at the start of the 20th century with two dozen colleges

of homeopathy and over 100 homeopathic hospitals throughout the United States. Scientific discoveries in bacteriology and disease processes that accompanied the turn of the century marked a turning point in the practice of medicine, however, and homeopathy soon went the way of bloodletting.

In the United States today practitioners of homeopathy typically learn the philosophy and methods through graduate classes during the course of their conventional education or through supplemental courses and programs they enroll in after completing their conventional education (though homeopathy is part of the regular curriculum for NATUROPATHY). However, because federal guidelines classify most homeopathic remedies as OVER-THE-COUNTER (OTC) DRUGS, they are available for anyone to purchase and use. Some remedies do contain ingredients that require a medical doctor's prescription. Surveys show that most of the 6 million Americans who use homeopathic remedies treat themselves without consulting a health-care practitioner.

Each state regulates the practice of homeopathy. In most states physicians (MD and DO), chiropractors (DC), naturopathic physicians (ND), and dentists (DDS and DMD) can make homeopathic diagnoses and prescribe homeopathic remedies. A few states have specific licensing requirements for MDs and DOs who also practice homeopathy. In Europe homeopathy remains a distinct discipline in health care, and homeopathic physicians receive specific training and credentialing.

Benefits and Risks of Homeopathy

Homeopathic remedies are so dilute, some as much as one part per million, that by conventional clinical standards they do not contain active ingredients. Because of this, they do not interact with other medications or cause side effects. Aside from the risks of improper manufacturing and potential contamination, health experts generally regard homeopathic remedies as safe, though some remedies contain significant quantities of alcohol. FDA regulations require homeopathic remedy labels to list the ingredients as well as the instructions for use (including conditions the remedy treats).

Health experts caution people to seek conventional medical care for symptoms that do not improve after five to seven days of treatment with homeopathic remedies, the same caution they extend for self-treatment with any over-the-counter product. Clinical studies of homeopathic remedies have produced mixed results, with some studies showing no greater effect than PLACEBO (an inactive substance) and others showing measurable improvement beyond placebo effect.

See also AROMATHERAPY; FLOWER ESSENCES.

human growth hormone (hGH) supplement A controversial anti-aging approach of injecting synthetic hGH to raise the body's natural levels of this HORMONE, known as growth hormone (GH) in its endogenous form (the form the body naturally produces). The PITUITARY GLAND produces endogenous GH. GH levels are highest in childhood and ADOLESCENCE, when the body is growing. GH stimulates this growth through various biochemical actions. GH levels stay fairly high through early to middle adulthood, during which time GH shifts its role to maintaining MUSCLE mass, BONE density, and cardiac STRENGTH (the HEART's ability to pump forcefully and efficiently). By about age 50, the pituitary gland produces less GH and levels in the bloodstream begin to decline. The characteristic physical changes of aging, such as increased body fat and decreased muscle mass, begin to manifest. OBESITY also slows hGH release.

Some children have deficiencies of GH, usually due to a tumor, endocrine disorder, or other dysfunction of the pituitary gland. GH deficiency in childhood and adolescence causes stunted growth and blocks many of the body's normal maturation processes. Some adults also have GH deficiencies; hGH supplementation similarly restores body levels to those needed for healthy muscles, bones, and cardiac function. Doctors have prescribed hGH supplementation to treat such deficiencies since the 1970s.

Many people who support hGH supplementation as an anti-aging measure point to the success of such treatments as evidence that hGH is safe. Some doctors agree that there is no difference between therapeutic hGH given to adults whose GH levels fall before age-related declines naturally take place; symptoms and response are the same. Other doctors question the therapeutic value of giving hGH to counter a process that seems purely

the result of the aging process rather than of a disease process. Proponents of hGH supplementation counter that reversing some of the effects of aging prevents age-related diseases, such as ATHEROSCLEROSIS and OSTEOARTHRITIS, from developing. This, they argue, is clearly a therapeutic effect. Those who question the safety of hGH supplementation note that researchers do not know the functions of GH in adults, or how GH influences factors such as body fat distribution and muscle mass. They further observe that though muscle mass increases with hGH supplementation in adults, muscle strength does not, raising more questions about the role of GH in the adult body. The debate touches on a number of key ethical issues that are not easy to resolve.

At present the US Food and Drug Administration (FDA) approves hGH supplementation only for people who have clinical GH deficiencies—that is, GH deficiencies resulting from pituitary dysfunction rather than aging. hGH supplement is available only with a doctor's prescription. Treatment with hGH supplement can cause HYPERTENSION, edema (fluid retention), and HEART FAILURE, and hGH supplement may interact with other hormone supplements such as thyroid and hydrocortisone. A rare but serious complication arising from too much GH is ACROMEGALY, in which the bones of the jaw, hands, and feet grow disproportionately large. Though the excessive growth stops when GH levels drop, changes that have already occurred are permanent.

HUMAN GROWTH HORMONE (HGH) SUPPLEMENT

Uses	Risks/Side Effects	Interactions
increase MUSCLE mass	ACROMEGALY	CORTISOL, hydrocortisone
decrease body fat	edema	thyroid supplement
improve cardiovascular function	HEART FAILURE	
prevent OSTEOPOROSIS		

See also ANTI-AGING APPROACHES; HORMONE THERAPY; POLYGLANDULAR DEFICIENCY SYNDROME.

hypnosis A method of induced deep relaxation, sometimes perceived as an altered state of CONSCIOUSNESS, in which a person often is more responsive to suggestion than during normal consciousness. Studies show changes in the patterns of electrical activity in the BRAIN when a person is under hypnosis, suggesting some parts of the brain become more active and others less active. Many people are able to recall details when hypnotized that they cannot otherwise remember. Though a person may not be able to recall a suggestion the hypnotherapist gives during hypnosis, he or she may act on the suggestion during full consciousness, often without full awareness.

FACTS ABOUT HYPNOSIS

- A person retains full control of his or her thoughts, emotions, and actions when under hypnosis.
- Hypnosis is fully voluntary. A person cannot be hypnotized against his or her will or without knowledge and participation.
- A person will not say or do anything, under hypnosis or as the result of hypnotic suggestion, that violates his or her values and sense of what is right and wrong.
- Some people do not respond to hypnosis or hypnotherapeutic suggestions, regardless of their willingness to do so.
- Most people fully remember everything that occurs under hypnosis.

Hypnotherapy may help people who are trying to make lifestyle changes such as in EATING HABITS or SMOKING CESSATION. It is also a clinically accepted method for managing chronic PAIN and stress. Sometimes people use hypnosis to help them visualize a state of health they desire to achieve, with the residual effect supporting them while they work toward their health goals. Such goals may include restoration of function after serious injury, weight loss, fitness level, and even REMISSION from CANCER. Hypnosis should always be an adjunct, not a primary, treatment; it accompanies and supports other therapies and treatments.

A typical hypnotherapy session takes place in a professional setting and may last 30 to 45 minutes. A person should emerge from hypnosis feeling refreshed and invigorated, fully capable of returning to the day's regular activities. Some circumstances may need several hypnotherapy sessions, though many require only a session or two. In addition to performing hypnosis, a hypnotherapist can teach self-hypnosis. Self-hypnosis may be helpful for reinforcing suggestions the hypnother-

apist provides during a hypnotherapy session. Self-hypnosis is also an effective stress relief method, particularly for people who have chronic health conditions that cause discomfort or pain. Often the hypnotherapist will make a recording of the first session for the person to replay at home.

A person who practices hypnosis may be a doctor, nurse, psychologist, psychotherapist, dentist, naturopathic physician, or certified hypnotist. Most states do not regulate hypnotherapy, so it is important to fully understand the hypnotherapist's education, credentials, and experience even when the hypnotherapist is a certified or licensed health practitioner. It is important to feel a high level of trust in the hypnotherapist. Hypnosis itself is generally a safe practice, though it can allow people to recall circumstances that are emotionally painful. Once those emotions surface, the person may need professional guidance to address them.

See also BIOFEEDBACK; MIND–BODY INTERACTIONS.

integrative medicine An approach to the practice of medicine that uses conventional and complementary therapies in conjunction with one another. In the United States integrative medicine typically refers to physicians (MDs and DOs) who practice conventional medicine that incorporates complementary therapies, such as ACUPUNCTURE and herbal remedies, or who work in close association with complementary practitioners such as massage therapists and chiropractors.

Doctors in the United States who practice integrative medicine typically use complementary methods that clinical studies have shown to provide therapeutic benefit or at the least have not shown to cause harm. Hospitals often use integrative methods such as MEDITATION and VISUALIZATION with people who are undergoing major surgery or CANCER treatment. The ORNISH PROGRAM for CARDIOVASCULAR DISEASE (CVD) presents an integrative approach that has obtained Medicare approval, a step that speaks to the effectiveness and acceptability of its methods.

See also HOMEOPATHY; MEDICINAL HERBS AND BOTANICALS; NATUROPATHY; TRADITIONAL CHINESE MEDICINE (TCM).

L

labyrinth A spirituality-based approach that features a geometric, symmetrical pattern that a person walks in prayer, MEDITATION, VISUALIZATION, or quiet contemplation. Many hospitals have labyrinths, which may be small or large, indoors or outdoors, permanent or temporary. The tradition of the labyrinth dates to medieval times and has integrated with a number of religious and spiritual practices through the centuries. The winding, convoluted path of the labyrinth physically and symbolically draws the person into the center. Once at the center, the person turns and follows the path back out. Many people experience profound calm and inner peace as they complete their labyrinth journeys. People who have chronic or terminal conditions often find the labyrinth gives them respite from their symptoms while within the labyrinth and often for hours to days afterward.

See also NATIVE AMERICAN HEALING; PRAYER AND SPIRITUALITY; REIKI; TRADITIONAL CHINESE MEDICINE (TCM).

lutein An ANTIOXIDANT belonging to the carotenoid family. Lutein, along with another carotenoid, ZEAXANTHIN, helps protect against AGE-RELATED MACULAR DEGENERATION (ARMD) and other retinal disorders. ARMD is the leading cause of progressive vision loss among adults. Some studies suggest lutein may also help lower the risk for LUNG CANCER. Ophthalmologists often recommend lutein in combination with ZEAXANTHIN, an antioxidant that occurs in many of the same foods as lutein, for people in middle age and older. There is limited evidence that lutein and other carotenoids may also help prevent cataracts from forming.

Lutein occurs naturally in the dark yellow pigments found in red bell peppers, pumpkin, and in dark green vegetables such as spinach and broccoli. It is also available as a dietary supplement, usually in combination with other carotenoids. Too much lutein or other carotenoids, which typically occurs only when taking high doses of carotenoid supplements, can cause the palms of the hands and soles of the feet to turn orange or dark yellow. This is a temporary effect that goes away when the amount of consumed carotenoids decreases. Penicillin-based ANTIBIOTIC MEDICATIONS may decrease lutein absorption.

LUTEIN

Uses	Risks/Side Effects	Interactions
prevent cataracts	excessive amounts may turn the palms and soles of the feet orange or dark yellow	none known
reserve macular function		
possibly protect against LUNG CANCER		

See also BILBERRY; CATARACT; CATARACT EXTRACTION AND LENS REPLACEMENT; LYCOPENE; RETINOPATHY; VITAMIN AND MINERAL THERAPY.

lycopene An ANTIOXIDANT that is one of the carotenoids. Lycopene emerged in the 1990s as an adjunct (secondary) therapy for PROSTATE CANCER because of its ability to slow the growth of prostate CANCER cells. It may also help to slow the growth of cancer cells in other locations, notably the LUNG and LIVER. In combination with LUTEIN and ZEAXANTHIN (other carotenoids), lycopene helps protect the RETINA and vision.

Lycopene occurs naturally in fruits and vegetables that have red flesh, such as tomatoes, guava, and watermelon. The highest levels of lycopene

occur in cooked tomatoes and tomato products such as tomato soup, tomato sauce, and ketchup. Most studies investigating the effects of lycopene involved consuming high amounts of foods containing lycopene, notably cooked tomato products. The findings seem to substantiate lycopene's role in inhibiting the growth of cancer cells, particularly prostate cancer cells. However, few research studies have evaluated lycopene supplements. Because tomatoes contain numerous nutrients, it is difficult to assess the effects of only one.

Most doctors agree that while there is likely little harm to come of taking lycopene supplements, there is not enough evidence to recommend doing so except as an adjunctive therapy (in addition to other therapeutic approaches). Men who have prostate disease or PROSTATE CANCER may benefit from increasing their consumption of foods containing cooked tomatoes. Excessive ingestion of lycopene and other carotenoids can cause the palms of the hands and the soles of the feet to turn dark yellow or orange, a temporary circumstance that returns to normal when carotenoid levels drop after stopping or reducing the supplement. There are no other known risks or side effects when using lycopene, though taking penicillin-based ANTIBIOTIC MEDICATIONS may decrease the amount of lycopene absorbed into the bloodstream from the gastrointestinal tract.

LYCOPENE

Uses	Risks/Side Effects	Interactions
prevent or slow PROSTATE CANCER possibly protect against LUNG CANCER preserve retinal function	excessive amounts may turn the palms and soles of the feet orange or dark yellow	none known

See also AGE-RELATED MACULAR DEGENERATION (ARMD); BILBERRY; CATARACT EXTRACTION AND REPLACEMENT; RETINOPATHY; SAW PALMETTO; VISION IMPAIRMENT; YOHIMBE/YOHIMBINE.

magnet therapy The use of static magnets to create magnetic energy fields, which are alignments of the atoms within them. The most common use of magnet therapy is to treat chronic PAIN such as from OSTEOARTHRITIS, RHEUMATOID ARTHRITIS, FIBROMYALGIA, and CARPAL TUNNEL SYNDROME.

People who have implanted medical devices such as pacemakers, defibrillators, and INSULIN pumps should not use therapeutic magnets because they may interfere with the electrical functions of the devices.

Therapeutic magnets come in many strengths and configurations, from adhesive-backed strips to items of jewelry such as necklaces and bracelets to magnets designed for placement under the mattress. The only aspects of magnet therapy that fall within regulatory reach are labeling and marketing. Because there are no clinical studies to support the therapeutic qualities of static magnets, the US Food and Drug Administration (FDA) prohibits therapeutic magnet manufacturers from claiming health benefits from their products. Magnet STRENGTH varies widely among manufacturers and products, and often varies from the stated strength on the product packaging.

MAGNETIC ENERGY MEASURES

Earth's magnetic field	0.5 gauss
refrigerator magnets	35 to 200 gauss
therapeutic magnets	300 to 5,000 gauss
MAGNETIC RESONANCE IMAGING (MRI) magnet	200,000 gauss

Source: National Center for Complementary and Alternative Medicine (NCCAM)

The earliest documented use of magnets for HEALING comes from medieval times, when surgeons used lodestones and magnets made from them to locate and remove iron fragments and arrowheads from soldiers on the battlefield. With understanding of the body's functions in health or disease considerably limited until the start of the twentieth century, magnets remained among the most popular tools in the doctor's medicine bag.

Though several theories for how magnets may exert therapeutic influence seem plausible, particularly because neurologic and other cellular functions generate electromagnetic fields. so far clinical studies have not produced findings that support them. A number of studies have shown therapeutic benefit with pulsed electromagnetic therapy, in which a rapidly pulsating electrical current creates a temporary, powerful magnetic field. Only health-care professionals may use electromagnetic therapeutic devices under current regulations in the United States.

Most health experts believe static magnets have very limited therapeutic effect though are not likely to cause harm in most people. Pregnant women (because effects of magnetic energy fields on a developing fetus remain unknown) and people who have implanted electronic devices (because the magnet may interfere with the device's electromagnetic field) should not use magnet therapy. Magnets cannot treat or cure diseases such as CANCER, DIABETES, and CARDIOVASCULAR DISEASE (CVD), though some disreputable vendors may represent them as being able to do so. A doctor should evaluate any condition that does not improve within 7 to 10 days.

See also ALTERNATIVE METHODS FOR PAIN RELIEF; BIOFEEDBACK FOR PAIN RELIEF; TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS).

massage therapy A touch therapy, also called therapeutic massage or bodywork, that acts on the body as well as the mind and the emotions. About 25 percent of people who seek massage therapy do so to relieve PAIN and stiffness related to musculoskeletal injuries, and a third are interested in stress relief. There are dozens of therapeutic massage techniques and methods, though all share the common intent of stimulating the flow of BLOOD through the muscles and soft tissues to cleanse metabolic toxins, tone MUSCLE tissues, and release tension.

Though a doctor may recommend massage therapy in conjunction with PHYSICAL THERAPY, the two have distinctly different approaches. Physical therapy is fix-oriented: there is a problem and massage can help make it better. Therapeutic massage in the context of physical therapy is one component of a treatment plan that might also include therapies such as hydrotherapy (whirlpool or soaking bath), ULTRASOUND, and electrotherapy (gentle stimulation of the muscles with mild electrical current). The treatment plan focuses on the injured body part, and the massage therapist or physical therapist does not usually massage other parts of the body.

INFANT MASSAGE

Many neonatal care units use massage therapy with premature infants. The gentle touch of the massage therapist seems to calm and relax these babies born before their bodies are quite ready to process the stress of external stimulation. Studies show that infants who receive massage therapy gain weight and grow faster, and go home earlier from the hospital.

Massage therapy independent of physical therapy has a holistic orientation, approaching manipulation of the body within the context that the body holds physical, emotional, and spiritual tension. The massage therapist may focus on a particular area of the body that he or she detects is holding more tension than other parts of the body. Though the intent is not necessarily one of HEALING a musculoskeletal injury, massage therapy typically results in improvement of FLEXIBILITY and mobility. When the muscles release stored physical tension, they often also release stored emotional tension. The result of this release can be quite profound. Many people begin to cry during massage therapy or find themselves recalling past experiences that caused them pain or grief. From a holistic perspective, this release is essential to healing in a broad context.

Massage therapy also facilitates the flow of lymph, helping the body to clear metabolic toxins stored in the muscles. Particularly in people who are sedentary, lymph flow may be sluggish. Chronic health conditions also may impair lymph circulation. People who have had lymph nodes surgically removed (lymphectomy) to treat cancer may have gaps in the lymph circulatory structures; massage therapy helps LYMPH to work around those areas to restore its movement (lymphatic drainage). As the LYMPHATIC SYSTEM is key to immune function, stimulating lymph circulation improves resistance to illness and INFECTION.

In the United States, each state regulates the practice of massage therapy. Thirty states have specific education, training, and certification requirements. Health experts recommend that regardless of state standards, massage therapists should have passed the certification requirements of the National Certification Board for Therapeutic Massage and Bodywork (NCTBMB) and belong to the American Massage Therapy Association (AMTA). Naturopathic (NDs), CHIROPRACTIC (DCs), and osteopathic physicians (DOs) are among the practitioners who most often also have formal training in massage therapy. In addition to an individual's credentials, however, the most important factors in selecting a massage therapist are trust and comfort.

See also LYMPHEDEMA; REFLEXOLOGY; REIKI.

medicinal herbs and botanicals Plants have been the source of HEALING therapies for all of known history and among all societies. The earliest written records across cultures make reference to teas, berries, salves pounded and mixed from leaves and barks, seeds, roots, and other plant parts as remedies for ailments ranging from HEADACHE to digestive upset to GOUT. The ubiquitous aspirin, whose chemical basis is salicylic acid, derives from the bark of the willow tree. For centuries Native Americans chewed this bark to

relieve TOOTHACHE, headache, and other pains, yet it was not until 1899 that researchers isolated and synthesized this key ingredient. About 30 percent of the drugs and medicines in use today derive from plant sources—the HEART medication digoxin from foxglove, for example, and the anticancer DRUG tamoxifen from the yew tree. Complementary and alternative therapies employ hundreds of plant-based remedies.

Effectiveness

Until the 1980s, there were few US clinical research studies to evaluate the benefits, risks, and effectiveness of botanical therapies, though European countries have conducted countless clinical studies. Germany's *Commission E Monographs*, a document that extensively documents the effectiveness and safety of more than 300 herbs and botanicals, stands as one of the definitive treatises on botanical remedies, analogous to Western medicine's pharmacopoeias. The Commission E updates the *Monographs* every few years as it completes investigation of additional products. Many practitioners around the world rely on the *Monographs* for information about benefits, risks, dosages, and forms of botanical therapies.

As interest has surged among Americans in using these therapies, US researchers have expanded their studies of them. Plant-based therapies in the research spotlight are PHYTOESTROGENS, for their effects in relieving hormonal discomforts related to MENOPAUSE and their potential ability to head off PROSTATE CANCER and BREAST CANCER, and SOY for its role in preserving cardiovascular health. Recent clinical studies have demonstrated the value of the herb BILBERRY to improve night vision and prevent cataracts, the herb MILK THISTLE to protect the LIVER's ability to restore itself, the herb ST. JOHN'S WORT to treat mild to moderate DEPRESSION, and the extract SAW PALMETTO to treat BENIGN PROSTATIC HYPERPLASIA (BPH).

Other remedies have failed to produce clinical evidence of their effectiveness, such as the herb DONG QUAI to treat HOT FLASHES and other discomforts of menopause. This does not mean the remedy is ineffective; it means only that so far researchers do not understand how the remedy functions in the body and cannot consistently reproduce the claimed beneficial results. Much research continues in the areas of botanicals and herbal remedies.

Forms and Preparations

The part of the plant from which the botanical product derives also affects its potency. Seeds and roots generally contain the highest concentrations of plant chemicals, while leaves or stems contain weaker concentrations. Common preparations of botanicals include the following:

- Extracts are made by soaking the plant in water to draw out its active ingredients, and the liquid becomes the product. Extracts also are evaporated out to leave the product in a powder form that manufacturers may package as loose powder or in capsules, or form into tablets.
- Tinctures are made by soaking the plant in ALCOHOL or a mixture of alcohol. The water draws out the active ingredients, and tinctures remain in liquid form.
- Teas are made from fresh, dried, or freeze-dried parts of the plant. Manufacturers may package them loose or in tea bags.
- Capsules contain powdered plant parts (usually extracts).
- Tablets are compressed powders containing the plant ingredients as well as inert binders and fillers.
- Liquids are usually extracts or decoctions in bottled form.

Most herbalists recommend staying as "close to the earth" as possible, using actual plant parts (fresh, dried, or extracted) rather than supplements manufactured from isolated ingredients.

Standardization

Medicinal botanicals have been in use in Europe for millennia, and strict standards now govern their manufacture and use in most European countries. Many require a doctor's prescription. In the United States, most medicinal botanicals and herbal preparations fall under minimal regulatory oversight as dietary supplements. The US Congress passed the Dietary Supplement Health and Education Act in 1994, allowing dietary supplement classification for any substance other than TOBACCO

that, according to the US National Institutes of Health (NIH) Office of Dietary Supplements

- has the intention to supplement dietary intake
- contains dietary ingredients such as vitamins, minerals, amino acids, or botanical substances, including herbs
- is taken in some form by MOUTH (such as liquid, tablet, capsule, gel, tea, freeze-dried, or powder) either by itself or mixed with food or water
- carries clear labeling on the front of the package that identifies the product as a dietary supplement

Further, dietary supplements may not make health claims unless the US Food and Drug Administration (FDA) approves them. Dietary supplements are thus exempt from the rigorous standards that medications must meet.

In the United States, there are no standards for product ingredients or consistency for dietary supplements, other than the product may not contain substances that the law prohibits or claim to contain ingredients that it does not. The term *standardized* on a dietary supplement label can mean anything the manufacturer desires, from consistency in following the same recipe and balance of ingredients in making every batch of the supplement to all tablets in the same bottle are the same color. Many manufacturers strive to produce supplements that have consistent ingredients and potency across batches though some do not. Though reading product labels for the percentages or measurements of included ingredients is helpful, health experts point out that because there are no standards to control those measurements, there is no way to know how accurate they are.

THE USP QUALITY STANDARD

The United States Pharmacopeia (USP) maintains a verification program of stringent guidelines to assure the quality of dietary supplements. Manufacturers whose products meet the quality guidelines may place the designation "USP" on product labels. The organization's Web site (www.usp.org) maintains a current list of USP-verified products.

Another factor affecting the consistency of botanical supplements manufactured from harvested plants (as opposed to synthesized ingredients) is the wide variation possible among the source plants. Soil conditions, mineral content of the water, the amounts of water and sunshine, the part of the world where the plant grows, and numerous other environmental factors influence the plant's growth and the potency of its active ingredients. The time and method of harvest also affects potency. As well, there may be different species of the plant, such as GINSENG (Siberian, Korean, Red, *Panax*), that have differing potencies and characteristics. Manufacturers may blend several species or use whatever species is available or less expensive.

Safety

There is a tendency to view herbs and botanicals as "safe" because they are natural. However, any substance that alters the functions of the body has the capacity to be both helpful and harmful. Foxglove provides digoxin, a medication that maintains heart rhythm and STRENGTH in millions of people. Foxglove also is one of the most potent poisons; the sap residue left on the fingers after picking its beautiful purple and white bell-like flowers is enough to cause life-threatening ARRHYTHMIA (disturbance of the heart's rate and rhythm) especially in children.

Herbal remedies, like conventional medications, can interact with each other as well as with conventional medications. Most herbal products available over-the-counter are mild formulas that generally are safe when people take them according to recommended guidelines or package instructions. Some herbal formulas are potent enough, or carry sufficient risk for harmful effects, that the FDA regulates them as drugs. An example is the "herbal Viagra" remedy YOHIMBE/YOHIMBINE, derived from the bark of the African yohimbe tree, which is available in the United States only with a doctor's prescription. It is important for doctors to know, when considering prescription medications, all of the remedies, including vitamin and mineral supplements, people are taking.

See also ALTERNATIVE AND COMPLEMENTARY REMEDIES FOR CANCER; TRADITIONAL CHINESE MEDICINE.

THERAPEUTIC BOTANICALS, HERBS, AND SUPPLEMENTS

Name	Common Uses/Benefits	Risks/Side Effects
BILBERRY *(Vaccinium myrtillus)*	improve night vision, prevent AGE-RELATED MACULAR DEGENERATION (ARMD), prevent cataracts, prevent RETINOPATHY of DIABETES	none known
BLACK COHOSH *(Actaea racemosa, Cimicifuga racemosa)*	relieve menopausal HOT FLASHES	can cause uterine contractions and interfere with oral contraceptives
BOSWELLIA *(Boswellia serrata)*	relieve pain of OSTEOARTHRITIS, RHEUMATOID ARTHRITIS, IRRITABLE BOWEL DISEASE (IBD), and other AUTOIMMUNE DISORDERS	none known
CHAMOMILE *(Matricaria recutita)*	relieve gastrointestinal upset, sleep aid, general relaxation	none known
CHONDROITIN	reduce INFLAMMATION and relieve PAIN of osteoarthritis may prevent or reverse damage to JOINT tissues	may interfere with actions of anticoagulant medications
COENZYME Q10	lower BLOOD PRESSURE, strengthen force of HEART's contractions, help heart to recover after HEART ATTACK, prevent PERIODONTITIS may prevent cancers and chronic health conditions related to oxidation	none known
DONG QUAI *(Angelica sinensis)*	relieve menstrual cramps, menopausal discomforts, and ENDOMETRIOSIS symptoms	may cause STOMACH irritation and excessive menstrual bleeding may interfere with actions of anticoagulant medications and NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)
ECHINACEA *(Echinacea angustifolia, Echinacea pallida, Echinacea purpurea)*	prevent or reduce symptoms of upper respiratory infections such as COLDS and INFLUENZA (flu) general IMMUNE SYSTEM support	none known
FEVERFEW *(Tanacetum parthenium)*	relieve migraine HEADACHE and menstrual discomfort	may cause excessive bleeding may interfere with anticoagulant medications, aspirin, and NSAIDs
GARLIC *(Allium sativum)*	lower BLOOD cholesterol and risk for ATHEROSCLEROSIS, CORONARY ARTERY DISEASE (CAD), and PERIPHERAL VASCULAR DISEASE (PVD)	interferes with many antihypertensive medications may cause excessive bleeding with surgery

Name	Common Uses/Benefits	Risks/Side Effects
GINGER *(Zingiber officinale)*	relieve general NAUSEA, nausea of CHEMOTHERAPY, MORNING SICKNESS, motion sickness, and digestive upset	may interfere with anticoagulant medications and ASPIRIN THERAPY may cause excessive bleeding
GINKGO BILOBA	relieve symptoms of RAYNAUD'S SYNDROME, INTERMITTENT CLAUDICATION, and ALZHEIMER'S DISEASE may improve PVD, CAD, and atherosclerosis	interferes with numerous medications including anticoagulants, antihypertensives, thiazide diuretics, prochlorperazine, trazodone interferes with aspirin therapy
GINSENG *(Panax ginseng, Panax quinquefolius)*	improved mental clarity and focus, memory general immune system support improved INSULIN sensitivity aphrodisiac	interferes with loop diuretics can result in excitability and insomnia when combined with CAFFEINE
GLUCOSAMINE	reduce inflammation and relieve pain of osteoarthritis relieve chronic BACK PAIN may prevent or reverse damage to joint tissues	may cause gastrointestinal upset interferes with loop diuretics
GOLDENSEAL *(Hydrastis canadensis)*	topical and systemic antibiotic general immune system support relieve digestive upset relieve and help heal canker sores increase resistance to URINARY TRACT INFECTION (UTI)	none known
GREEN TEA *(Camellia sinensis)*	prevent development and spread of CANCER lower low-density lipoprotein (LDL) cholesterol improve circulation strengthen TEETH and resist bacterial MOUTH infections	contains significant amount of caffeine
LUTEIN	preserve macular structure and function, protect vision, prevent cataracts	none known
LYCOPENE	prevent development and spread of PROSTATE CANCER preserve retinal function and protect vision	none known
MELATONIN	relieve insomnia prevent jet lag alter sleep patterns to accommodate shift work	causes strong drowsiness numerous medication interactions may raise blood pressure should not take with diabetes, CARDIOVASCULAR DISEASE (CVD), kidney disease

Name	Common Uses/Benefits	Risks/Side Effects
MILK THISTLE *(Silybum marianum)*	protect the LIVER from damage due to CIRRHOSIS, chronic HEPATITIS, mushroom poisoning, and DRUG poisoning	interferes with insulin therapy for diabetes
PHYTOESTROGENS	relieve menopausal discomforts and PREMENSTRUAL SYNDROME (PMS) symptoms lower blood cholesterol enhance BONE DENSITY and STRENGTH to prevent osteoporosis possibly prevent prostate cancer and some kinds of BREAST CANCER	may diminish fertility may increase risk of certain kinds of breast cancer
SAMe (S-adenosylmethionine)	relieve mild to moderate DEPRESSION relieve symptoms of osteoarthritis, back pain, and CHRONIC FATIGUE SYNDROME	may cause insomnia and gastrointestinal upset interferes with monoamine oxidase inhibitor (MAOI) antidepressants
SAW PALMETTO *(Sabal serrulata)*	stop PROSTATE GLAND from enlarging relieve symptoms of benign PROSTATIC HYPERPLASIA (BPH)	may interfere with some treatment for prostate cancer
soy	lower LDL cholesterol, reduce risk for CAD reduce risk for osteoporosis, prostate cancer, and certain breast cancers relieve menopausal discomforts, especially hot flashes	may cause gastrointestinal upset may increase risk for certain estrogen-driven breast cancers
ST. JOHN'S WORT *(hypericum perforatum)*	relieve mild to moderate depression	increases sensitivity to the sun and ultraviolet light interferes with some chemotherapy agents, HIV/AIDS medications, immunosuppressive drugs, and selective serotonin reuptake inhibitor (SSRI) and MAOI antidepressants
SUN'S SOUP	slow metastasis of non-small cell LUNG CANCER (NSCLC) reduce HIV/AIDS symptoms and progression	none known
VALERIAN *(Valeriana officinalis)*	sleep aid relieves anxiety	may cause excessive drowsiness in combination with other substances and medications that also cause drowsiness
YOHIMBE/YOHIMBINE *(Pausinystalia yohimbe)*	treat ERECTILE DYSFUNCTION aphrodisiac	may cause elevated blood pressure interferes with MAOI antidepressants interacts with foods containing tyramine

Name	Common Uses/Benefits	Risks/Side Effects
ZEAXANTHIN	prevent cataracts preserve macular function and protect vision possibly protect against LUNG CANCER and OVARIAN CANCER	none known

meditation A method of focusing the mind for HEALING VISUALIZATION, relaxation, stress relief, and contemplation. Though meditation can have a spiritual dimension for people who desire it, meditation is not a religious practice. Clinical studies show that daily meditation has the ability to

- reduce EPINEPHRINE production, thereby lowering BLOOD PRESSURE and the frequency of ANGINA PECTORIS
- relax BLOOD vessels, which also lowers blood pressure
- relax musculoskeletal structures
- instill a sense of inner calm and peacefulness
- decrease the frequency, duration, and severity of menopausal HOT FLASHES

When meditation becomes a routine of daily life, these effects can help lower blood pressure by reducing the resistance blood encounters as it flows through the arteries. They also increase the flow of blood to muscles, helping muscle cells to more efficiently clear lactic acid accumulations and other metabolic wastes that cause cramping and discomfort. Some people use meditation as a platform to "go within" their bodies and visualize healthy, strong cells, tissues, organs, and functions. Such visualization may aid in healing during illness or injury as well as in maintaining health.

There are many methods of meditation. Meditation centers, YOGA centers, community centers, and health organizations often teach classes in meditation techniques. Meditation may take place while sitting quietly, while walking, or while engaged in mind–body practices such as yoga and TAI CHI. Some people chant when meditating, to focus their meditations with specific sounds or intents. Though a quiet location best facilitates meditation, a person can meditate anywhere. Many people take five-minute meditation breaks while at work to help dissipate job stress. Children also can learn to meditate. Meditation has no known health risks.

See also MIND–BODY INTERACTIONS; PRAYER AND SPIRITUALITY; STRESS AND STRESS MANAGEMENT.

melatonin An endogenous (naturally occurring within the body) HORMONE the PINEAL GLAND produces that maintains the body's circadian rhythms (cycles of waking and sleeping). Melatonin may also have ANTIOXIDANT functions, helping protect cells from damage. Researchers first discovered melatonin in the late 1950s, and early studies suggested endogenous melatonin (melatonin the body manufactures) production diminished with increasing age. This gave rise to speculation that melatonin played a role in the aging process. Subsequent studies have been unable to substantiate such involvement, however, and most doctors do not believe melatonin can halt, prevent, or reverse aging.

The daily level of melatonin in the body cycles a pattern of peaking between 2 o'clock and 4 o'clock in the morning (which is the middle of the night for most people) and reaching its lowest point around midday. Researchers believe the HYPOTHALAMUS, a structure deep within the BRAIN that regulates vital body functions such as BREATHING and BLOOD PRESSURE, receives signals from the RETINA via the OPTIC NERVE that indicate whether it is light or dark. When it is dark, the hypothalamus signals the pineal gland to begin releasing melatonin and when it is light, to stop releasing melatonin. This may in part explain why people feel drowsy when spending several hours in dark settings such as movie theaters, or want to go to sleep earlier in the winter when daylight is short and have trouble falling asleep in summer when daylight is much longer.

Raising the level of melatonin in the bloodstream increases drowsiness, which has led to the use of melatonin supplement as a sleep aid. In the United States melatonin is available as an over-the-counter dietary supplement. In most European countries, however, melatonin is available only with a doctor's prescription. This is because researchers do not fully understand the functions of melatonin in the body though they do know that as a hormone, melatonin has numerous effects within the body in addition to the roles it plays in sleep cycles and the circadian rhythm. Some studies have found that melatonin causes blood vessels to constrict, perhaps by stimulating the release of CORTISOL, raising blood pressure. Though this finding is not conclusive, health experts advise people who have HYPERTENSION (as well as people who have other forms of CARDIOVASCULAR DISEASE (CVD), DIABETES, and KIDNEY disease) not to take melatonin to avoid this risk.

A number of studies support melatonin's ability to relieve jet lag and help people adjust to sleeping during the day when they work during the night. However, there are no studies that conclusively identify supplemental melatonin's benefits or risks. Melatonin interacts with numerous prescription medications and should be taken only after a doctor's examination determines there are no neurologic or other physiologic causes for insomnia. Even people taking melatonin for jet lag or to restructure their sleep patterns to accommodate shift work should first consult with their doctors to make sure they have no health conditions that make it unsafe for them to take melatonin supplements.

Melatonin causes drowsiness within 20 to 30 minutes of taking a DOSE, an effect that lasts four to six hours. Some people experience a "hangover" effect when they wake up, feeling groggy and disoriented for as long as several hours. People must not drive or operate machinery after taking a melatonin dose, as the onset of sleepiness can be sudden and irresistible. Some people also experience increased insomnia or have vivid dreams and nightmares as well as fatigue after taking melatonin. Melatonin taken in combination with other medications that cause drowsiness can result in an intensified effect (excessive sleepiness).

MELATONIN

Uses	Risks/Side Effects	Interactions
sleep aid	drowsiness	CORTICOSTEROID MEDICATIONS
	possible fertility problems	prescription sleep aids
	may elevate BLOOD PRESSURE	ASTHMA medications
	insomnia	ANTIHISTAMINE MEDICATIONS
	fatigue	narcotic ANALGESIC MEDICATIONS
		ANTIANXIETY MEDICATIONS
		MUSCLE RELAXANT MEDICATIONS
		ANTIDEPRESSANT MEDICATIONS

See also ANTI-AGING APPROACHES; SLEEP DISORDERS; VALERIAN.

milk thistle A medicinal herb, also called holy thistle, that helps protect the LIVER from INFECTION and improves the liver's ability to regenerate from damage. Numerous clinical studies support this benefit. The active ingredient in milk thistle is silymarin, a composite of five flavonoids (siliandrin, silibinin, silydianin, silymonin, and silychristin), which is in highest concentrations in the milk thistle seeds. Silymarin strengthens the structure of hepatocytes, the cells in the liver that metabolize toxins. It may also influence aminotransferases, the enzymes the liver produces to break down chemical substances the liver extracts from the blood.

Doctors often recommend milk thistle for people who have LIVER DISEASE OF ALCOHOLISM, CIRRHOSIS, or chronic HEPATITIS, or who have ingested toxic mushrooms or toxic doses of medications such as acetaminophen. Some people who have HIV/AIDS take milk thistle or silymarin extract to protect their livers from the potentially damaging effects of some of the medications used to treat HIV/AIDS. There also is limited evidence that milk thistle has a similarly protective function in the kidneys though researchers continue to explore this possible effect. A folk medicine use for milk thistle, likely the origin of the plant's name, is to stimulate BREAST milk production in nursing mothers. Of the few studies that have investigated this use, there have been no conclusive findings about benefits or risks. Because the effects are unknown,

health experts recommend BREASTFEEDING mothers do *not* use milk thistle or silymarin extract.

Milk thistle is available in dried plant form in teas, and also in preparations of silymarin extract in tablet form. People who are allergic to common thistle, daisies, artichokes, or kiwi (all of which are in the same plant family as milk thistle) should not take milk thistle or silymarin in any form. Milk thistle or silymarin extract may cause digestive upset including NAUSEA and DIARRHEA. Because of its enzymatic inhibitory actions, milk thistle may interfere with INSULIN–GLUCOSE processes. People who have DIABETES should consult with their doctors before using milk thistle or silymarin.

MILK THISTLE *(Silybum marianum)*

Uses	Risks/Side Effects	Interactions
CIRRHOSIS	allergic reaction	INSULIN therapy
chronic HEPATITIS	digestive upset	
mushroom poisoning		
DRUG poisoning		

See also HEPATOTOXINS.

mind–body interactions Approaches of care that engage the interrelationships between the mind and the body for HEALING and health. Healers have known for centuries that the state of the mind influences the condition of the body. Contemporary physicians will not hesitate to say that the patient's attitude and outlook are at least as important as any technology modern medicine has to offer. Though the mind alone cannot prevent or heal significant physical conditions such as CANCER or CARDIOVASCULAR DISEASE (CVD), an individual's mindset shapes the determination with which he or she approaches treatment and treatment's ultimate success or failure.

MIND–BODY THERAPIES

AROMATHERAPY	ART THERAPY
BIOFEEDBACK	CRANIOSACRAL MASSAGE
HYPNOSIS	MASSAGE THERAPY
MEDITATION	PRAYER AND SPIRITUALITY
REIKI	TAI CHI
VISUALIZATION	YOGA

At the most basic level, perceptions about health, illness, and the success or failure of treatment influence a person's compliance with the doctor's recommendations from the taking of prescription medications to lifestyle modifications such as weight loss or SMOKING CESSATION. At a more sophisticated level, clinical studies demonstrate the ability of some people to consciously alter body functions such as HEART RATE and BLOOD PRESSURE through methods such as BIOFEEDBACK and MEDITATION. Cancer treatment programs use healing visualization, in which the person in treatment meditates to visualize his or her cancer gone and the body strong and healthy. Surgeons and anesthesiologists often recommend visualization before and after surgery, encouraging people to "see" the surgery succeed and the body restore itself to health.

See also BEHAVIOR MODIFICATION THERAPY; LIFESTYLE AND HEALTH; ORNISH PROGRAM.

N–O

Native American healing A spirituality-based approach, also called traditional North American medicine, that incorporates ceremony, ritual, and symbolism. In the Native American tradition, intent is as important as action and there are no distinctions between body, mind, and spirit. The illness or health of one affects the well-being of the whole. As well, traditional Native American medicine holds that HEALING takes place within the body's sense of time and timing, and efforts to rush or otherwise influence this timing extend rather than shorten the healing process.

Traditional Native American healing practices made use of the sweat lodge, a small enclosed structure in which a fire burned hot. The heat would flush the cause of the ailment to the surface, where it would manifest in the form of a vision. People stayed in the sweat lodge until the heat initiated within them the vision necessary for healing. The person might then go into the forest, desert, or mountains to be with the vision and allow the natural environment to reveal its meanings. The experience also restores the balance between the individual and the natural environment, an essential component of the healing process from the traditional perspective.

Some hospitals in areas where there are Native American populations are beginning to incorporate Native American healers among the complementary providers available to patients, notably in the American Southwest. Drumming, chanting, smudging, and dancing may be among the elements of healing rituals. One of the most common ceremonies is the medicine wheel, a form of ritual MEDITATION or prayer similar to a LABYRINTH. The circle of the wheel represents the continuous harmony of the universe, with the four spokes representing the four directions and their correlations to body (north), spirit (south), mind (east), and inner peace (west).

See also AYURVEDA; MIND–BODY INTERACTIONS; PRAYER AND SPIRITUALITY; TRADITIONAL CHINESE MEDICINE (TCM).

naturopathy A system of medicine that uses methods and substances found in nature to maintain and restore health. The philosophical foundation of naturopathy rejects interventions such as major surgery, RADIATION THERAPY, and drugs other than elements, minerals, and other natural compounds. Naturopathy incorporates or supports therapeutic approaches such as ACUPUNCTURE, energy medicine, NUTRITIONAL THERAPY using diagnostic testing through functional medicine, hydrotherapy, physiotherapy, MEDICINAL HERBS AND BOTANICALS, HOMEOPATHY, and manipulative therapies (such as CHIROPRACTIC, MASSAGE THERAPY, and OSTEOPATHIC MANIPULATIVE TREATMENT [OMT]).

Naturopathic Diagnosis and Treatment

The naturopathic physician assesses symptoms and examines patients in much the same fashion as a conventional doctor, though spends considerably more time addressing lifestyle factors such as nutrition, activity, relationships, stress, and emotional well-being. The naturopathic physician may function as a consultant for botanical or nutritional therapies, or as a primary-care provider who works collaboratively with other health-care professionals and refers people for specialty care as needed, as would a conventional doctor (MD or DO). The naturopathic approach considers the person holistically and incorporates therapeutic methods that both treat symptoms and restore overall health and well-being. Naturopathic physicians spend much time educating people about

how to better manage their health to prevent illness.

Naturopathic Practitioners

Naturopathy traces its origins to ancient HEALING methods based entirely on natural methods, the only approach available for centuries. Today in the United States, naturopathic physicians complete comprehensive education and training programs and must pass licensing examinations in the states in which they practice. A naturopathic physician receives a doctor of naturopathy degree and puts the initials "ND" or "NMD" after his or her name. Many naturopaths have additional training and certification in ACUPUNCTURE and TRADITIONAL CHINESE MEDICINE (TCM), broadening the scope of their perspectives and abilities to accommodate diverse interests in health care among the people who come to them for care.

Benefits and Risks of Naturopathy

Naturopathy as practiced in the United States today functions synergistically with conventional therapies. The risks of naturopathic remedies vary according to the person's primary and secondary health conditions and with the therapeutic approach. Within such a context, and because naturopathy does not use medications or major surgery, naturopathy is overall less risky than conventional medicine. It is important for people to receive appropriate conventional medical treatments for conditions that require it, such as type 1 DIABETES. Herbal remedies can interact with each other as well as with conventional medications. A person who receives care from conventional as well as naturopathic doctors should be sure all practitioners know they are collectively participating in that care.

See also OSTEOPATHY; REFLEXOLOGY.

nutritional therapy A therapeutic approach that uses nutraceuticals, foods, vitamins, minerals, and special diets to fight disease and maintain health. Nutritional therapy as a complementary method is not the same as the NUTRITIONAL ASSESSMENT a registered dietitian (RD) might provide for compliance with conventional nutrition requirements. Nutritional therapy instead blends holistic concepts with dietary modifications.

From a conventional medicine perspective, the premise that nutrition and diet influence health and disease is not new or unique. Foods may contribute to numerous health conditions. Some foods energize and others relax the body. Foods also can be harmful to people who have certain medical conditions. For example, people who have HEMOCHROMATOSIS, a metabolic disorder that allows iron to accumulate in various organs, worsen the condition when they eat foods high in iron such as spinach. Food allergies, such as to peanuts, can have lethal consequences.

HEALTH CONDITIONS FOODS INFLUENCE

ANEMIA	ATHEROSCLEROSIS
ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)	AUTISM
CELIAC DISEASE (sprue)	CARDIOVASCULAR DISEASE (CVD)
chronic OTITIS media	ECZEMA
GASTROESOPHAGEAL REFLUX DISORDER (GERD)	GOUT
INFLAMMATORY BOWEL DISEASE (IBD)	HEMOCHROMATOSIS
migraine HEADACHE	IRRITABLE BOWEL SYNDROME (IBS)
OBESITY	multiple metabolic syndrome
OSTEOARTHRITIS	OSTEOPOROSIS
PREMENSTRUAL SYNDROME (PMS)	PSORIASIS
RECURRENT YEAST INFECTIONS	RHINITIS
type 2 DIABETES	WILSON'S DISEASE

Many of the most significant health conditions facing Americans today in some way relate to EATING HABITS. Many people eat too much in general, too much of foods that do not support health, or not enough foods that provide the body with the nutritional foundation it needs to meet its energy and maintenance requirements. The most compelling evidence of this is the OBESITY rate in the United States; more than two thirds of Americans are overweight (5 to 20 percent above healthy weight) and nearly a third have obesity (20 percent or higher above healthy weight). Of special concern is the significant rise in the number of children who have obesity, particularly children under 10 years old. Some studies also link dietary habits with health conditions such as COLORECTAL CANCER.

Because many people do not eat nutritiously, dietary changes to improve nutrition nearly always

result in health improvements. However, the scientific connections between nutrition and health or disease are not entirely clear and sometimes appear even conflicting. As yet, there are very few circumstances (other than those that are the direct result of nutritional deficiencies) in which consuming or not consuming certain foods can prevent health conditions. Foods, and the nutrients they contain, certainly can support wellness or contribute to disease. But nutritional therapy that restricts or emphasizes certain nutrients may create nutritional deficiencies and imbalances.

See also ALTERNATIVE AND COMPLEMENTARY REMEDIES FOR CANCER; DRUG INTERACTIONS; LIFESTYLE AND HEALTH; MALNUTRITION; NUTRITIONAL NEEDS; NUTRITIONAL SUPPLEMENTS.

osteopathic manipulative treatment (OMT) A touch therapy that uses pressure, stretching, and manipulation of the muscles and joints to relieve musculoskeletal discomfort. The goal of OMT is to release restrictions within musculoskeletal structures to restore FLEXIBILITY and mobility. OMT may improve chronic BACK PAIN, FIBROMYALGIA, CHRONIC FATIGUE SYNDROME (CFS), and REPETITIVE MOTION INJURIES such as CARPAL TUNNEL SYNDROME, and ROTATOR CUFF IMPINGEMENT SYNDROME. OMT represents one of the founding principles of OSTEOPATHY, that the structure of the body supports the body's health. Often, a doctor of osteopathy (DO) has the training and expertise to perform OMT.

See also ALTERNATIVE METHODS FOR PAIN RELIEF; CHIROPRACTIC; JOINT; MASSAGE THERAPY; MUSCLE; REFLEXOLOGY.

osteopathy A philosophy of health care that emphasizes preventive approaches and self-care to manage lifestyle choices in ways that encourage wellness. Osteopathy strives to support the structures of the body to maintain health. In the United States, a doctor of osteopathy (DO) has the same practicing privileges and licensing requirements as a medical doctor (MD) and is considered a conventional physician. The osteopathic medicine curriculum is comparable to the curriculum at a conventional medical school, typically a four-year graduate program with a subsequent internship and residency though with more opportunity to learn manipulations such as OSTEOPATHIC MANIPULATIVE TREATMENT (OMT) and craniosacral massage. Though many osteopathic physicians choose to practice in primary care, they may become specialists in any area of medicine.

See also AYURVEDA; HOMEOPATHY; NATUROPATHY; OSTEOPATHIC MANIPULATIVE TREATMENT; REFLEXOLOGY; TRADITIONAL CHINESE MEDICINE (TCM).

P–R

phytoestrogens Plant-based ESTROGENS, many of which are similar in chemical structure to the estrogens the human body produces. In plants, phytoestrogens are part of the botanical IMMUNE SYSTEM, helping protect the plant from fungal and bacterial INFECTION. In humans, phytoestrogens exert a weak estrogenic effect relative to that of endogenous (produced within the body) or supplemental estrogen. Though an abundance of research supports numerous health benefits from eating foods high in phytoestrogens, questions remain about the effectiveness of phytoestrogens in supplement forms as well as the precise mechanisms and consequences of them in the human body.

DIETARY SOURCES OF PHYTOESTROGENS

Isoflavones	Lignans	Coumestans
soybeans	flaxseed	red clover
SOY-based foods	flaxseed oil	pinto beans
red clover	lentils	lima beans
textured vegetable protein	carrots	split peas
soy protein isolate	oat bran	alfalfa sprouts
soy milk	oatmeal	red clover sprouts
licorice	asparagus	

There are two main classifications of phytoestrogens: isoflavonoids (isoflavones) and lignans. Soybeans are the primary source of isoflavones such as genistein and daidzien, and nuts and flax are the primary sources of lignans. A third classification of phytoestrogens, coumestans, appears to have an even stronger estrogen effect in the body though research has not focused on them. Red clover and alfalfa, especially sprouts, contain coumestans. Most plants have combinations of phytoestrogens with one that is dominant. Supplements prepared from extracts of these substances often combine the various phytoestrogens into formulas for specific uses, such as MENOPAUSE symptoms or DYSMENORRHEA (difficult menstrual periods or menstrual cramps).

The primary therapeutic uses for phytoestrogens are to improve the discomforts of PREMENSTRUAL SYNDROME (PMS) and menopause. Some studies support the value of some phytoestrogens, notably isoflavones, in preventing or limiting PROSTATE CANCER and BREAST CANCER though health experts do not agree on the extent to which these actions result from the isoflavones. Studies using isoflavone extracts in supplement form produce less conclusive findings than those studies that use isoflavone-containing (SOY-based) foods. Isoflavones may also help reduce the risk for CARDIOVASCULAR DISEASE (CVD) by lowering blood cholesterol levels and for OSTEOPOROSIS by aiding the bones in retaining calcium. Some studies show soy has limited ability to slow osteoclastic activity (bone destruction) and promote osteoblastic activity (bone construction).

Because their chemical structures are similar to those of endogenous estrogens, phytoestrogens are able to bind with estrogen receptors (specialized molecular "switches" in cells) in the body. However, the bond is an incomplete fit and more fragile than the bond of endogenous or supplemental estrogen, and produces a weaker estrogen response. Health experts disagree on the role this weaker bond and response may play in reducing the risk for breast cancer in women. Some believe phytoestrogens, because they occupy estrogen receptors, prevent more potent endogenous estrogen from binding and thus suppress estrogen availability. Less estrogen means less fuel for potential CANCER cells, theoretically inhibiting their ability to manifest as breast cancer.

Other health experts worry that by only partially blocking estrogen effect in the body, phytoestrogens allow other chemical communications to take place that could actually increase the risk for estrogen-driven breast cancers in some women who have previously had estrogen-driven breast cancer. However, it remains unclear whether endogenous estrogen binding creates a greater risk. Some studies show a stronger preventive effect in premenopausal women and a less conclusive preventive effect in postmenopausal women, which researchers correlate to the differences in the kinds of breast cancers likely to affect each age group. Research continues to explore these issues, and doctors remain divided in their recommendations. Many health experts recommend obtaining phytoestrogens through natural food sources rather than supplements, to receive the additional benefits of other nutrients in the foods.

PHYTOESTROGENS

Uses	Risks/Side Effects	Interactions
relieve MENOPAUSE discomforts relieve PREMENSTRUAL SYNDROME lower blood cholesterol enhance BONE calcium possibly prevent BREAST CANCER possibly prevent PROSTATE CANCER	fertility disturbances possible increased risk of breast cancer in certain women	none known

See also BLACK COHOSH; DONG QUAI; SOY AND CARDIOVASCULAR HEALTH.

prayer and spirituality Faith-based approaches to HEALING. Numerous anecdotal reports as well as clinical studies support a connection between healing and belief practices such as prayer and spiritual MEDITATION. Researchers at Duke University's Center for Spirituality, Theology, and Health have conducted a number of studies measuring different immune function indicators in people who regularly attend religious services and in people who do not. Over time, researchers found, the immune systems of people who regularly participate in religious or spiritual activities (regardless of belief system) have higher levels of INTERLEUKINS and other immune factors.

Two thirds of American medical schools now teach courses in prayer and spirituality, and all hospitals have chaplains on staff or clergy on call. Most hospitals have chapels or meditation rooms for where patients can go privately, as well as locations where family members and friends may gather to pray or meditate. Many people participate in prayer circles, through churches or through other common structures, in which they pray specifically for others who are injured or ill. A number of studies suggest that the beneficiaries of these prayers, called intercessory prayers, tend to improve more quickly. In degenerative conditions such as ALZHEIMER'S DISEASE, the ritual of shared spiritual or religious practices often provides comfort and a sense of stability. Spiritual practices also help provide a sense of meaning and acceptance when health conditions are terminal.

See also END OF LIFE CONCERNS; NATIVE AMERICAN HEALING; SPIRITUAL BELIEFS AND HEALTH CARE.

qigong See TRADITIONAL CHINESE MEDICINE (TCM).

reflexology A therapeutic approach that uses massage and pressure on the feet and hands. The philosophy of reflexology holds that the soles of the feet (and to lesser extent, the palms of the hands) contain reflex points that correlate to body structures and functions. Activating these points affects the correlating structure or function, relieving energy blockages that might be causing symptoms or disease. People receiving reflexology treatments often experience the pressure of the reflexologist's touch as well as tingling or other sensations in the area of the body that correlates with the reflex point.

The sole of each foot contains more than 7,000 NERVE endings. Nerve pathways branch through various regions of the body on their way to or from the SPINAL CORD and BRAIN. One theory for how reflexology might work is that activating a nerve ending such as on the bottom of the foot could result in a nerve response elsewhere along the path of the nerve structure. Other theories correlate reflexology to energy channels and net-

works similar to those of ACUPUNCTURE (though acupuncture and reflexology are not related in philosophy or practice). However, there are no clinical studies to substantiate any of these theories, or that reflexology produces objective results. Most conventional doctors are skeptical that reflexology has therapeutic value beyond that which one might expect from a thorough foot massage.

See also MASSAGE THERAPY; REIKI.

Reiki A 3,000 year-old system of energy HEALING that originated with Tibetan monks. The word *Reiki* means "universal life force." Reiki practitioners use their hands, without touching the person, to focus energy. The energy might come from the person's body, identifying the location of illness or injury. Sometimes the Reiki practitioner experiences these locations as feeling hot or cold. The energy also comes through the Reiki practitioner to the person, focusing healing where the body needs it. Many people feel profound relaxation and release during a Reiki session and often relief from PAIN. It is common for both the person receiving Reiki and the Reiki practitioner to emerge from a Reiki session feeling a heightened sense of awareness.

Because there is no clinical substantiation for the effects of Reiki, many doctors tend to be skeptical. However, there are no known risks associated with Reiki when it is a complementary component of overall care and treatment. Unlike MASSAGE THERAPY, with Reiki there is no, or only very light, touching. The primary concern of conventional doctors is that people continue to receive conventional medical care when necessary.

A number of hospitals make Reiki practitioners available to people who are waiting for transplant organs or undergoing strenuous CANCER treatment. Some conventional health-care practitioners, such as nurses, become Reiki practitioners. Some researchers believe the deep relaxation that people experience with Reiki sessions causes the body to release natural PAIN-relieving chemicals (endorphins and enkephalins), accounting for effects such as pain relief and stress reduction. Reiki may be especially helpful for people who have conditions, such as BURNS or major trauma, that make touch therapies difficult or unfeasible.

Reiki practitioners designate their levels of expertise according to degrees. A first-degree Reiki practitioner has received basic Reiki training, typically a two-day session. A second-degree Reiki practitioner has been practicing Reiki for a minimum of three months and has completed an additional Reiki training session, typically a two-day workshop, to learn more advanced techniques including mental healing and distance healing. A third-degree Reiki practitioner is a Reiki master. A Reiki master has practiced Reiki for at least a year and then has completed a year-long training program. Reiki masters also teach Reiki. As with other forms of bodywork and energy healing, it is essential to trust in, and feel comfortable with, the Reiki practitioner.

See also ACUPUNCTURE; REFLEXOLOGY.

S

SAMe A chemical that occurs naturally in the BRAIN. SAMe, which is short for S-adenosylmethionine, participates in the brain's synthesis of DOPAMINE and serotonin, neurotransmitters that have key functions in brain communication regarding emotions and mood. SAMe is available in the United States as a dietary supplement and as a prescription medication in most European countries. People commonly take SAMe to relieve symptoms of DEPRESSION, OSTEOARTHRITIS, chronic BACK PAIN, and CHRONIC FATIGUE SYNDROME (CFS). Clinical studies support SAMe's effectiveness in treating depression and osteoarthritis, though are not entirely conclusive. So far research findings have failed to support a conclusive benefit from SAMe for chronic back pain and CFS.

Depression

In a number of clinical studies SAMe appears as effective as prescription tricyclic ANTIDEPRESSANT MEDICATIONS for treating mild to moderate depression and without the side effects, such as drowsiness and dry mouth, common to them. However, depression can be a serious medical condition. Doctors worry that people who use over-the-counter remedies to self-treat depression may put themselves at risk. Conventional medical approaches to treating depression may incorporate antidepressant medications with PSYCHOTHERAPY to resolve the underlying causes of the depression.

As well, any substance that alters the production and ratio of brain neurotransmitters has the potential to create imbalances in those vital brain chemicals that cause further problems. One such consequence is serotonin syndrome, a serious and potentially fatal accumulation of serotonin in the brain. SAMe appears to suppress monoamine oxidase, the same NEUROTRANSMITTER that tricyclic antidepressants target. While doctors monitor people taking tricyclics for evidence of serotonin syndrome, a person who is self-medicating with SAMe may not recognize the symptoms of serotonin toxicity (HEADACHE, dizziness, vomiting, disorientation and confusion, unconsciousness) as related to SAMe. Also because of SAMe's monoamine oxidase inhibition ability, people who are taking monoamine oxidase inhibitor (MAOI) antidepressants should not take SAMe.

Serotonin syndrome is a serious and potentially fatal SIDE EFFECT of ANTIDEPRESSANT MEDICATIONS. It requires immediate medical attention.

Osteoarthritis

A number of clinical research studies show that osteoarthritis improves after taking SAMe for four to six weeks. However, researchers have yet to identify the actions of SAMe responsible for this improvement. The METABOLISM of endogenous (naturally occurring) SAMe produces various chemical substances (notably amino acids) that the body can use to repair JOINT tissues and produce the synovial fluid that lubricates joints. Some researchers believe SAMe as a supplement provides more of these amino acids. Because of the length of time it takes to see improvement, however, other researchers question whether it is the SAMe supplement or the natural processes of the body that result in reduced PAIN and INFLAMMATION.

Chronic Back Pain and CFS

Chronic back pain and CFS can be debilitating conditions that defy attempts to improve symptoms. The mechanisms of both are poorly under-

stood, though theories abound. Most doctors feel that low doses of SAMe do no harm and thus are worth trying if they might bring improvement. The precautions that apply to other uses of SAMe remain pertinent. People taking SAMe for chronic back pain or CFS should do so only with the knowledge of their doctors, to avoid any possible interactions with prescription medications and to monitor for adverse effects or further deterioration of the underlying condition.

SAMe

Uses	Risks/Side Effects	Interactions
DEPRESSION	serotonin syndrome	MAOI antidepressants
OSTEOARTHRITIS	gastrointestinal upset	
chronic BACK PAIN	insomnia	
CHRONIC FATIGUE SYNDROME		

See also CHONDROITIN; GLUCOSAMINE; ST. JOHN'S WORT.

saw palmetto A botanical preparation made from the berries of the saw palmetto tree (*Sabal serrulata*) native to the American coastal southwest. Saw palmetto prevents the PROSTATE GLAND from enlarging, though it does not appear to reduce enlargement that has already occurred. Though many people believe saw palmetto can prevent PROSTATE CANCER, so far there is no conclusive evidence to support this effect.

Researchers do not know for certain what ingredients in saw palmetto have an active effect, though believe its fatty acids contain substances that mildly suppress TESTOSTERONE and its precursors (chemicals the body converts to testosterone). This action reduces testosterone levels enough to inhibit the growth of prostate cells but not so much as to cause other symptoms related to low testosterone such as diminished LIBIDO or ERECTILE DYSFUNCTION. Such symptoms are common with conventional medications such as finasteride (Proscar) to treat BENIGN PROSTATIC HYPERPLASIA (BPH), a condition affecting about half of men over age 60. Many doctors recommend a trial of saw palmetto before moving to finasteride, as saw palmetto is significantly less expensive as well as less likely to cause undesired side effects.

Men who take saw palmetto for BPH should have an annual prostate examination to check for early signs of prostate cancer. Saw palmetto is available in numerous formulations as dietary supplements, many of which include other ingredients. Health experts recommend choosing products that contain 90 to 95 percent saw palmetto sterol oils or fatty acids. Combination products may not contain enough saw palmetto to be effective. Saw palmetto can cause gastrointestinal distress; doctors recommend taking it with meals. Men who have prostate cancer should take saw palmetto only if their doctors approve; saw palmetto may interfere with some hormone-based prostate cancer treatments.

SAW PALMETTO *(Sabal serrulata)*

Uses	Risks/Side Effects	Interactions
stop PROSTATE gland enlargement	stomach upset	some PROSTATE CANCER treatments
relieve BPH symptoms		

See also AGING, URINARY SYSTEM CHANGES THAT OCCUR WITH; LYCOPENE; PROSTATE HEALTH; PROSTATITIS.

soy Researchers have noticed since the 1970s that people whose diets include soybeans and soy-based foods such as tofu have lower blood cholesterol levels and lower rates of CARDIOVASCULAR DISEASE (CVD). Numerous research studies have isolated various soy proteins such as genistein and daidzein that have demonstrated their ability to decrease low-density lipoprotein (LDL) cholesterol. The US Food and Drug Administration (FDA), which regulates the health claims manufacturers may make about their products, allows manufacturers to tout this effect on products that contain 25 grams or more of soy protein.

FOOD SOURCES OF SOY

immature soybeans (edemame)	mature soybeans
roasted soy nuts	textured vegetable protein (TVP)
tofu	dried soybeans
miso	soymilk
tempeh	soy flakes
soy protein isolate	
soy cheese	

The primary active ingredients in soybeans are PHYTOESTROGENS, chemicals that function in the human body like weak ESTROGENS. Researchers have connected estrogen with numerous health conditions including BREAST CANCER, PROSTATE CANCER, cardiovascular disease, and OSTEOPOROSIS. Though soy and phytoestrogens appear to improve these conditions, researchers remain uncertain as to the mechanisms of phytoestrogens in the human body and the potential risks that they present. Estrogen can both prevent and cause BREAST cancer, for example. Much research continues to explore these issues. In the meantime, health experts recommend most people substitute soy products for meats to reduce dietary saturated fats as a measure for reducing the risk of heart disease. Soybeans are the only plant-based source of complete protein, providing all of the essential proteins the body requires.

SOY

Uses	Risks/Side Effects	Interactions
lower LDL cholesterol	may increase risk for estrogen-driven breast cancers	none known
reduce risk for HEART disease	gastrointestinal upset	
reduce risk for OSTEOPOROSIS		
relieve menopausal discomforts		
reduce risk for PROSTATE CANCER		
reduce risk for some BREAST CANCERS		

See also GREEN TEA; HORMONE-DRIVEN CANCERS; HORMONE THERAPY; SOY AND CARDIOVASCULAR HEALTH.

St. John's wort An herb, *Hypericum perforatum,* that healers have used for centuries to treat DEPRESSION. The actions of St. John's wort appear similar to those of the serotonin reuptake inhibitor (SSRI) antidepressants. St. John's wort is available in teas, extracts, and capsules as a dietary supplement in the United States, and as a medication that requires a doctor's prescription in most of Europe. In Europe, St. John's wort is the most widely prescribed of the ANTIDEPRESSANT MEDICATIONS. Researchers believe the active ingredients are hypericin and hyperforin, though in isolation these substances do not produce the same results as the intact herb. These are the substances most commonly available in extract products.

Most health experts agree that while St. John's wort may help mild to moderate depression as well as mild to moderate anxiety, it is not effective in major depression or in BIPOLAR DISORDER, a combination of depressive and manic symptoms. St. John's wort interacts with a number of medications, including some HIV/AIDS medications, certain CHEMOTHERAPY agents, and IMMUNOSUPPRESSIVE MEDICATIONS such as cyclosporine taken following ORGAN TRANSPLANTATION. Because St. John's wort extends the presence and action of serotonin, people who take SSRI or monoamine oxidase inhibitor (MAOI) antidepressants should not take St. John's wort. A serious and sometimes fatal complication, serotonin syndrome, may result.

Serotonin syndrome is a serious and potentially fatal SIDE EFFECT of ANTIDEPRESSANT MEDICATIONS. It requires immediate medical attention.

Because depression can be a serious medical condition, most doctors prefer that people receive conventional medical treatment. That treatment may include St. John's wort, after a thorough evaluation of the person's physical and mental health status. But health experts caution that self-diagnosis and self-treatment can be risky.

ST. JOHN'S WORT *(Hypericum perforatum)*

Uses	Risks/Side Effects	Interactions
mild to moderate DEPRESSION	serotonin syndrome	CHEMOTHERAPY agents
	sun sensitivity	HIV/AIDS medications
		immunosuppressive drugs
		SSRIs and MAOIs

See also SAMe; VALERIAN.

Sun's Soup A formula of herbs and vegetables, formally called Sun Farms Vegetable Soup (SFVS) and sometimes referred to as Selected Vegetables, developed to treat non-small cell LUNG CANCER (NSCLC) and HIV/AIDS. The formula's developer,

Alexander Sun, a biochemist and former researcher at Yale and Mount Sinai schools of medicine, selected ingredients that appear to have cancer-fighting properties.

Though the actual formula is proprietary, published reports identify the original ingredients as shiitake mushrooms, mung beans, hawthorn fruit, onion, GINGER, American GINSENG, lentils, leeks, and the Chinese herbs bai hua she she cao and ban zhi lian. Sun's Soup comes in freeze-dried packages that the person mixes with hot water or hot soup once daily. In several small clinical studies with people who had moderate to advanced NSCLC, Sun's Soup produced measurable improvements. However, the small study size limited the value of the findings. Researchers are continuing to evaluate Sun's Soup in its various formulations.

There appear to be few side effects with Sun's Soup, with the primary complaints being dissatisfaction with the taste and gastrointestinal upset. As with other complementary therapies, it is important to continue appropriate conventional treatments. The conditions Sun's Soup targets, NSCLC and AIDS, are very serious diseases. Though there are few cures with NSCLC and there is no known cure for AIDS, there are treatments that prolong life and improve QUALITY OF LIFE.

See also NUTRITIONAL THERAPY; TRADITIONAL CHINESE MEDICINE (TCM).

T

tai chi A gentle form of martial art that features slow, fluid movements (called forms) combined with MEDITATION. Tai chi forms represent imagery found in nature. Tai chi improves balance, STRENGTH, FLEXIBILITY, and breath control. Most people participate in tai chi in groups with a leader (master) who guides the session's movements and length, though some choose to do tai chi as a solitary practice. Many community centers, health clubs, programs for seniors, and sometimes colleges offer tai chi classes.

A typical tai chi session may take 10 minutes to an hour, depending on the form. Most people begin a tai chi session with a few minutes of meditation and BREATHING EXERCISES to help cleanse the body and focus the thoughts. Sometimes the focus on performing the motions of the form is its own meditation, and sometimes the person has a specific meditative focus that he or she holds for the duration of the session. Though tai chi is not typically aerobic because its movements are so slow, it does stretch and exercise the entire body. Often tai chi groups meet outdoors, and some people like to do tai chi barefoot to symbolically and tangibly connect themselves with the Earth and nature.

Anyone of any age can benefit from tai chi as a meditation practice and for improved balance and coordination. Doctors often recommend tai chi for people who

- are older and have increased risk for age-related falls, to help prevent injuries such as fractured hip
- have chronic health conditions such as OSTEOARTHRITIS or RHEUMATOID ARTHRITIS that threaten to restrict mobility
- have degenerative conditions such as PARKINSON'S DISEASE or MULTIPLE SCLEROSIS, to maintain as much mobility as possible for as long as possible
- have ALZHEIMER'S DISEASE, to encourage social engagement and for the sense of comfort that the routine of tai chi imparts
- have CARDIOVASCULAR DISEASE (CVD) such as HYPERTENSION (high BLOOD PRESSURE), ATHEROSCLEROSIS, mild to moderate HEART FAILURE, or PERIPHERAL VASCULAR DISEASE (PVD), to improve blood flow and strengthen the HEART
- have OBESITY or are overweight and need a mild method to ease back into physical activity
- have CEREBRAL PALSY or other congenital disorders that affect coordination and movement

Because tai chi's movements are slow and gentle, there are few risks for most people. A tai chi master can help individuals modify tai chi forms to accommodate specific limitations and needs. People who have significantly impaired balance should do tai chi only in a group or with a partner, in case they do stumble or fall. Medications that cause drowsiness may decrease stability and balance. Most people feel relaxed yet invigorated following a tai chi session.

See also HIP FRACTURE IN OLDER ADULTS; TRADITIONAL CHINESE MEDICINE (TCM); YOGA.

therapeutic massage See MASSAGE THERAPY.

traditional Chinese medicine (TCM) A philosophy of holistic HEALING that dates to about 100 B.C.E., anchored in the premise that the energy that sustains the universe also sustains the body. Energy in balance is health; energy in imbalance is illness. Disease reflects blockages of energy that TCM therapies attempt to clear. The primary

energy balances are yin and yang, reflecting dual qualities of hot and cold, dark and light, male and female, and so on. TCM also draws from the five elements of nature—fire, earth, water, metal, and wood—and symbolic representations of organ systems. TCM's primary therapeutic approaches are herbal remedies and ACUPUNCTURE.

TCM physicians, also called doctors of Oriental medicine (OMDs), complete experience-based programs of study in which they serve in an apprentice fashion with a practicing TCM physician. Many of the written guidelines TCM physicians follow today derive from texts nearly as old as the practice of TCM itself, updated to accommodate modern knowledge and methods. Some states in the United States require specific licensing for TCM physicians and others for acupuncturists. A few states limit the practice of acupuncture to conventional health-care practitioners.

The TCM Physician's Examination

The TCM physician's examination differs from a conventional physician's examination in that there is considerable focus on factors such as posture, SKIN texture and tone, and how a person handles or carries his or her body. These factors often reveal to the TCM physician where and how the body's energy channels are blocked. The TCM physician also closely examines the tongue, from which TCM derives information about the state of the body's energy balances and blockages. The TCM physician also checks the PULSE at numerous points, some of which are not conventional pulse points. The TCM physician also asks many questions about the symptoms, how the person feels (physically and emotionally), the person's life experiences and circumstances, and in general listens closely to what the person describes and explains. TCM diagnoses blend symptoms, energy balance and imbalance, and the elements with perceptions of the affected organ systems and their functions. Treatments then undertake to release energy blockages to restore the flow of energy to organ systems and throughout the body.

Acupuncture

Acupuncture is a key therapeutic form in TCM. In traditional acupuncture, the TCM physician inserts hair-thin needles into specific points along energy channels called meridians. In the United States, TCM physicians and other acupuncturists use sterile, single-use needles. The needles, according to TCM, redirect the flow of energy. Contemporary Western medicine, which also incorporates acupuncture for treating chronic PAIN, ADDICTION, and other conditions, views the placement of needles as stimulating electrochemical responses in the NERVE endings. The process is painless, though some people feel a tingling sensation.

The TCM physician may place the needles in locations considerably distanced from the affected organs. For example, numerous acupuncture points on the outer EAR correlate to structures throughout the body. The outer ear is also the primary location for acupuncture points related to addiction. The needles typically stay in place for 20 to 30 minutes. Simple or acute conditions may require one to three treatment sessions; chronic or complex conditions may require a number of sessions over a period of weeks. Seldom does a condition require more than 12 treatments in total.

Chinese Herbal Remedies

Chinese herbal remedies derive from ancient recipes handed down through generations and generations of practitioners. They are precise measures of specific herbs, in specific preparations and intended for use exactly as the TCM physician prescribes, and there are thousands of different formulas as well as custom preparations that blend specific herbs into a combination to meet an individual's health needs. The remedies typically have Chinese names that reflect either the herbs they contain or the effects they are intended to achieve. Major remedies have four groups of herbs to treat four levels of the condition. The order in which the herbalist mixes the herbs together has symbolic significance that is as important as the herbs themselves. Major remedies have an emperor, minister, assistant, and envoy.

Most Chinese herbal remedies, when experienced and knowledgeable herbalists prepare them, are safe to take as the physician prescribes. Many herbal combinations contain potent ingredients and can evoke strong responses. It is important to know the source of the herbs as some herbs that come from directly from China may contain heavy metal contamination. Some herbs interact with

medications, so the person always should tell the TCM physician of any medications he or she is taking. Similarly, a person taking conventional medications should first discuss Chinese herbal remedies with his or her doctor before taking the remedies.

Moxibustion

Moxibustion is a technique for heating an herbal remedy, which the TCM physician often rolls into a wicklike structure and holds just above the skin while the herbs burn. The heat further stimulates the acupuncture point below the herb, drawing the herb's healing qualities into the body's meridians (energy channels) to release stubborn energy blockages. The TCM physician may combine moxibustion with cupping, in which the physician places a small glass cup over the skin while it is still warm. The cup contains the heat, which sucks the skin surface into the cup. This also intensifies the herb's actions.

Qigong

Qigong is a form of energy work that employs structured breathing, meditation, and physical movements, similar to TAI CHI or YOGA. Qigong is an integral aspect of nearly all TCM treatment approaches because it emphasizes balancing the flow of energy. The movements and BREATHING stimulate the flow of blood as well as the LYMPH circulation, helping clear toxins and metabolic wastes more quickly from the body. Many people practice qigong privately as they would MEDITATION. The movements are more simple than those of tai chi or yoga, and easier to learn from videotapes or books. Conventional doctors may recommend qigong separate from TCM as a means of improving balance, FLEXIBILITY, and mobility in people who are elderly or who have chronic health conditions that make movement difficult.

Many communities have classes in qigong, and some hospitals use it as part of their rehabilitation programs or for stress relief. Qigong is gentle and rhythmic, providing a sense of calm and relaxation at the same time that it tones and stretches the muscles and joints. Qigong is especially helpful for people who have conditions that restrict mobility, because its regular practice improves flexibility and range of motion.

Benefits and Risks of TCM

When practiced as a complementary approach, TCM offers considerable benefits without many risks. As with all alternative and complementary methods, conventional doctors become concerned when people forgo proven conventional treatments in lieu of alternative practices. TCM methods are not proven to cure HEART disease, CANCER, DIABETES, and other such conditions. Most TCM physicians in the United States are accustomed to working in close coordination with conventional practitioners, and refer people for conventional care for conditions that require it.

See also AYURVEDA; NATIVE AMERICAN HEALING.

V

valerian A medicinal herb (*Valeriana officinalis*) that causes drowsiness and relaxation, commonly taken as a sleep aid. Until the twentieth century physicians also used valerian for seizures, to relieve anxiety, for mild sedation, and as a diuretic. The valerian root, or rhizome, contains the highest concentration of active ingredients and is the source of medicinal preparations. Though valerian has an unpleasant taste and smell, herbalists recommend the tea, brewed from freshly harvested or freeze-dried rhizomes, for optimal benefit. Other forms, including capsules and tablets containing ground valerian root, are also available as dietary supplements in the United States.

VALERIAN *(Valeriana officinalis)*

Uses	Risks/Side Effects	Interactions
insomnia	excessive drowsiness	other sleep aids or medications
relieve anxiety		narcotic ANALGESIC MEDICATIONS
		ANTIANXIETY MEDICATIONS
		ANTIDEPRESSANT MEDICATIONS
		ANTIHISTAMINE MEDICATIONS
		MUSCLE RELAXANT MEDICATIONS

Efforts to isolate valerian's active ingredients have so far eluded researchers, though a number of clinical studies affirm its effectiveness as a mild sedative and sleep aid. Health experts recommend using valerian, like any other sleep aid, for no longer than two weeks. A doctor should evaluate sleep disturbances that continue longer. People who are taking other medications that cause drowsiness should not take valerian. ALCOHOL consumption also intensifies the drowsiness effect. There are no known health risks associated with valerian, though women who are pregnant or BREASTFEEDING should not take it because doctors and researchers do not know what effects, if any, it might have on the developing fetus or newborn infant.

See also GENERAL ANXIETY DISORDER (GAD); MELATONIN; SLEEP DISORDERS.

visualization A form of MEDITATION in which the person envisions his or her desired state of health or a treatment outcome such as surgery. Hospital surgery programs, CANCER recovery programs, and hospice programs began to integrate visualization methods in the 1990s. Many people find it calming and comforting to visualize themselves as healthy and whole, and many practitioners believe such visualization improves recovery rates and levels. Some people prefer guided imagery, in which a practitioner offers suggested visualizations and guides the person through the visualization process. Other people prefer to establish their own visualizations, and may integrate them with PRAYER AND SPIRITUALITY practices.

See also BIOFEEDBACK; LABYRINTH; MIND–BODY INTERACTIONS; NATIVE AMERICAN HEALING.

vitamin and mineral therapy Doses of vitamins and minerals that are higher than those typically recommended for health maintenance. Vitamin and mineral therapy derives from the perspective that depletions of vital nutrients are the primary cause of disease and that preventing these depletions can prevent the health concerns. Vitamin and mineral therapy in this context differs from routine vitamin supplementation and treatments that target specific nutritional deficiencies.

Vitamins and minerals are important nutrients the body needs to carry out its many functions. All such nutrients the body needs exist in nature and typically enter the body through foods and drinks. Even drinking water contains numerous minerals. Most people in the United States obtain adequate amounts of vitamins and minerals through appropriate dietary choices, despite concerns that the American diet on the whole is less than ideal to support health. People who live in areas where certain essential nutrients are lacking, such as selenium, which occurs in specific kinds of soil and the foods grown in them, may need to take supplements to acquire adequate amounts of those nutrients. Women who menstruate monthly may need supplemental iron to replace that lost to menstrual bleeding, and health recommendations call for supplementation of calcium and other key minerals at age 50 and older to maintain BONE density.

Conventional health experts are divided about whether healthy adults need or benefit from additional vitamins and nutrients. Some believe the ANTIOXIDANT actions of vitamins helps to prevent chronic diseases that result from cumulative damage to cells from free radicals, molecular particles that are the waste products of OXYGENATION functions (the ways in which cells metabolize nutrients to produce energy). Clinical research studies have produced conflicting results about antioxidants, however, and there remains little scientific evidence that they prevent disease or the degeneration associated with aging.

The body requires fairly small amounts of many minerals and vitamins to meet its functional needs, and excretes or stores any excess. Accumulations of certain vitamins, such as the fat-soluble vitamins A and E, may become toxic and cause health problems. Excessive mineral consumption (sodium, potassium, calcium, magnesium) can affect the body's electrolyte balance, consequentially altering KIDNEY function, cardiovascular function, and NERVOUS SYSTEM function with potentially harmful or life-threatening outcomes. The body excretes excess water-soluble vitamins (the B vitamins and vitamin C), so ingesting more than the body needs has no value. Researchers have established nutritional value ranges for most identified nutrients.

Nonetheless, many complementary approaches incorporate moderate to high doses of certain vitamins and minerals, depending on the person's symptoms. Health experts urge caution, and suggest a comprehensive NUTRITIONAL ASSESSMENT before beginning any intensive vitamin and mineral therapy. Pregnant or BREASTFEEDING women and people receiving treatment for chronic or degenerative health conditions who take regular medications should consult with their doctors, as some medications and vitamins interact to alter the action of one or the other or both. Practitioners such as naturopathic physicians and chiropractors often incorporate vitamin and mineral therapy in their practices.

See also DRUG INTERACTIONS; NUTRITIONAL THERAPY.

Y–Z

yoga A 5,000-year old practice originating in China that blends exercise and MEDITATION. Yoga incorporates specific configurations of the body called poses. Many poses are gentle and easy for most people to perform regardless of fitness level or expertise with yoga, and some poses are complex and difficult for the novice or the unconditioned to perform. Some poses are static (the person moves into and holds the pose) and some are dynamic (moving). There are several kinds of yoga. The yoga most Americans practice is Hatha yoga and its derivations. Astanga yoga, also called power yoga, is highly aerobic and requires a good FITNESS LEVEL. Some people chant during yoga, while others meditate quietly.

The essence of yoga is breath control, which ancient practitioners believed was the connection among body, mind, and spirit. Every yoga pose incorporates patterned, structured BREATHING. There are dozens of such breathing patterns, which a person also can perform independent of the yoga postures that employ them. Pulmonary care specialists often recommend yogic breathing for people who have chronic LUNG diseases or who are recovering from extensive injuries or surgery. Yogic breathing emphasizes opening the full body to the breath, and uses methods that help the body to extract more oxygen from each breath.

People who have musculoskeletal conditions such as chronic BACK PAIN or REPETITIVE MOTION INJURIES often experience pronounced benefits from yoga. Yoga can help such conditions heal by increasing blood flow to the area and by gently stretching, toning, and strengthening the involved musculoskeletal structures. Athletes may use specific yoga poses to stretch and warm up before practices, events, and competitions. Pregnant women, particularly those in the third trimester of pregnancy, often find yoga an effective way to stay fit and relieve stress. A yoga instructor can help an individual select poses specifically for his or her condition as well as modify poses to accommodate any limitations.

Health clubs, community centers, and private yoga instructors offer classes and sessions in yoga in many communities throughout the United States. Numerous books and videotapes also can teach yoga poses, though most people benefit from having a qualified yoga instructor observe their poses and help them get them right. Even the basic poses are precise in how they position and hold the body, and doing them incorrectly lessens the benefit and may cause discomfort or injury. There are no health risks associated with properly performed yoga poses.

See also TAI CHI.

yohimbe/yohimbine An herbal preparation from the bark of the African yohimbe tree (*Pausinystalia yohimbe*) taken to improve erectile function in men or as a treatment for ERECTILE DYSFUNCTION. Yohimbe may also produce a mild sense of euphoria, resulting in its reputation as an aphrodisiac. In the United States yohimbe is marketed as a dietary supplement and available without a doctor's prescription. The active ingredient in yohimbe is yohimbine. Yohimbine is available as a concentrated extract, which is much more potent than herbal yohimbe, and requires a doctor's prescription.

People sometimes call yohimbe "herbal Viagra," a reference to the prescription medication (sildenafil) for erectile dysfunction. Yohimbine,

yohimbe's active ingredient, works in somewhat similar fashion to sildenafil in that causes an increase in the body's production of NOREPHINEPHRINE which in turn increases the flow of blood to the PENIS. Norepinephrine has numerous other effects on cardiovascular function, including BLOOD PRESSURE and HEART RATE, so the US Food and Drug Administration (FDA) restricts the amount of it that is permissible in over-the-counter products.

Most health experts feel the amount of yohimbine, and thus the amount of norepinephrine, in over-the-counter yohimbe herbal remedies is too low to have a physiologic effect. They recommend that men instead see their doctors when erectile dysfunction is a concern, to identify any physical problems that might be responsible as well as to discuss options for treatment. The doctor can write a prescription for the more potent yohimbine extract if that is an appropriate therapeutic approach. Common causes of erectile dysfunction include ATHEROSCLEROSIS and PERIPHERAL VASCULAR DISEASE (PVD) resulting from CARDIOVASCULAR DISEASE (CVD) or DIABETES. Treating these underlying conditions often improves erectile function at the same time that it improves overall health. Men who have these conditions, or who take antihypertensive medications to treat HYPERTENSION (high blood pressure) generally should not take yohimbe and yohimbine products.

Yohimbe and yohimbine also block the actions of the NEUROTRANSMITTER monoamine oxidase, which may account for the mild euphoria some people experience when taking yohimbe-derived products. Monoamine oxidase affects BRAIN activity related to mood and emotion. Men who are taking monoamine oxidase inhibitor (MAOI) medications, either as ANTIDEPRESSANT MEDICATIONS or as treatment for PARKINSON'S DISEASE, should not use yohimbe products. Men who do use yohimbe products should avoid foods containing the amino acid tyramine, which requires monoamine oxidase for METABOLISM. Excess tyramine can produce numerous unpleasant symptoms, including severe HEADACHE and possible extreme spikes in blood pressure that could result in STROKE. Foods that contain tyramine include red wines, smoked meats and fish, aged cheeses, and dark chocolate.

YOHIMBE (PAUSINYSTALIA YOHIMBE)

Uses	Risks/Side Effects	Interactions
aphrodisiac ERECTILE DYSFUNCTION	elevated BLOOD PRESSURE	MAOI medications tyramine in foods

See also AROMATHERAPY; GINKGO BILOBA; LIBIDO; SAW PALMETTO.

zeaxanthin An ANTIOXIDANT that is one of the carotenoids. Zeaxanthin helps protect the health of the RETINA and to prevent AGE-RELATED MACULAR DEGENERATION (ARMD). Ophthalmologists often recommend zeanthin in combination with another carotenoid, LUTEIN, for people who are middle-aged and older. These antioxidants are present in the cells of the retina, where they absorb blue light that can damage the retina. As an antioxidant, zeaxanthin helps the retinal cells rid themselves of metabolic waste. Some studies suggest zeaxanthin and lutein may also help prevent cataracts from forming in the EYE'S LENS.

ZEAXANTHIN

Uses	Risks/Side Effects	Interactions
prevent CATARACT preserve macular function possibly protect against LUNG CANCER possibly protect against OVARIAN CANCER	excessive amounts may turn the palms and soles of the feet orange or dark yellow	none known

Foods that contain zeaxanthin include dark leafy vegetables such as spinach, collard greens, broccoli, and kale. Yellow fruits and vegetables such as peaches, mangoes, squash, and corn also contain zeaxanthin. Many of the foods that are rich in zeaxanthin also contain lutein and other carotenoids. As an antioxidant, zeaxanthin may also protect against certain cancers, notably LUNG CANCER and OVARIAN CANCER. In supplement form, zeaxanthin typically appears in products that are blended carotenoids. Carotenoids appear to have

greater effect in combination rather than in isolation, which is how they occur in nature, despite their individual actions and benefits.

People who take excessive amounts of carotenoid supplements may find the palms of their hands and soles of their feet take on a yellowish orange discoloration. This is a temporary effect that wears off when stopping the supplement allows the amounts of carotenoids present in the body to decrease. Taking zeaxanthin with foods that contain some fat increases the amount of zeaxanthin that enters the bloodstream from the digestive tract. Taking penicillin-based ANTIBIOTIC MEDICATIONS may decrease zeaxanthin absorption.

See also BILBERRY; LYCOPENE; PHYTOESTROGENS; RETINOPATHY.

GENETICS AND MOLECULAR MEDICINE

Genetics and molecular medicine are the disciplines in health care that focus on genetic encoding and molecular function within the cell as the foundations for health and disease. Many medical researchers believe nearly every component of health—and correspondingly, every presentation of disease—has some degree of genetic involvement and an individual acquires whatever propensity toward health that his or her genes convey. The manifestations of health and disease in many situations then become a combination of genetics and environment (lifestyle factors). The specialists who diagnose and treat GENETIC DISORDERS *are geneticists.*

This section, "Genetics and Molecular Medicine," presents an overview discussion of the structures and functions of human genetics and entries about genetic health and disorders. The entries in this section focus on genetic consequences for health across the spectrum of the body as a whole, including disorders and diseases that affect multiple systems. Entries in other sections of *The Facts On File Encyclopedia of Health and Medicine* provide detailed content about conditions that result from genetic disorders that affect single body systems. Cross-references connect entries with one another.

Structures of Genetics

GENE/ALLELE
CHROMOSOME
DNA
RNA

cell
- nucleus
- cytoplasm
- ribosome
- mitochondrion

molecule

Functions of Genetics

Genetics determines every aspect of human existence, from appearance and structure to function. Each individual acquires one set of chromosomes, the molecular presentation of heredity, from each parent. Each complete complement of chromosomes (23 pairs) contains 25,000 to 30,000 genes, the smallest structural and functional units of heredity. Each GENE pair within the structure of a CHROMOSOME has a single and specific task. It accomplishes this task by instructing the cell to make a particular protein, a process called protein encoding. Through protein encoding genes direct every action of every cell.

The genome: the book of life The complete complement of chromosomes is the human GENOME, quite literally the book of life. The genome contains all of the instructions the body requires to take shape and to function. Within a single individual, every one of the body's 100 trillion cells contains the same set of chromosomes, so all cells in the body read from the same book of life.

DNA (deoxyribonucleic acid) is the ink of the genome, the biochemical substance that allows the GENETIC CODE to express itself. DNA organizes itself in chemical presentations called nucleotides, which function somewhat like letters. Human DNA presents a surprisingly brief alphabet for the extensive range of genetic expression it permits, forming only four NUCLEOTIDE compounds that subsequently shape the 30,000 or so genes the human genome contains. One of the most intriguing discoveries of the HUMAN GENOME PROJECT is that there are vast amounts of "empty" DNA. Only 1 to 2 percent of DNA encodes. The remaining 98 to 99 percent of DNA is noncoding, much like white space on the printed page of a book. Researchers believe noncoding DNA somehow stabilizes or in other ways supports the structure of DNA within the chromosomes.

Each gene, like a word, contains patterns of nucleotides. Chromosomes, like sentences and paragraphs, present strings of genes that convey integrated and coordinated sets of instructions for specific structures and functions throughout the body. Collectively these genetic instructions are the pages, written in code, that form an individual's GENOTYPE. The outcome, the individual's outward presentation of his or her genetic code from appearance to health, is the PHENOTYPE.

Decoding the messages: the cells The cells decode, interpret, and implement an individual's genotype. Each gene carries an encoded message that it transcribes to RNA (ribonucleic acid), a carrier molecule within the cell. The RNA conveys the gene's message to the cell's ribosomes. Ribosomes are organelles (defined structures with specific functions) within the cell. The job of the ribosome is to translate the gene's message into a specific protein. The protein then carries the message to its target within the body, which is usually molecular.

Transmitting the code: inheritance patterns The function of conveying a genotype is as much one of mathematics as biology. INHERITANCE PATTERNS—the ways in which genes reorganize into new pairs at CONCEPTION—are the patterns of statistics. A geneticist can calculate with astonishing accuracy the likelihood of certain traits passing from parents to offspring. Such calculations accommodate the potential combinations that can arise from each parent's genotype.

Health and Disorders of Genetics

In some respects what is perhaps most remarkable about human genetics is the precision and consistency with which myriad, intricate, and complex biochemical actions take place not only to produce a new human being but also to choreograph its functions for eight decades or longer. Though everyone's genotype contains some mutations, researchers believe most mutations have no consequence for the body's structure or function. However, understanding of the complex interactions among genes continues to evolve as geneticists engage in further research.

It is a common misperception that there are genes that cause disease, such that there are specific genes for HEMOPHILIA or CYSTIC FIBROSIS in the same fashion as there are certain genes for brown HAIR or green eyes. There are not really "disease" genes, however. There are instead flaws and errors in the structures of certain genes (mutations) that cause them to give the wrong instructions for synthesizing their specific proteins. The consequence is a gap, expansion, or rearrangement in the information. In some situations a gene, or more commonly a segment of or an entire chromosome, is missing—as if pages or chapters are torn from the genetic book of life. In other situations the gene may have extra material or its material is rearranged—as if pages or chapters are inserted into the book. The resulting errors in structure or function can be quite significant.

IDENTIFIED GENETIC AND MOLECULAR DISORDERS

ALPORT SYNDROME
CONGENITAL HEART DISEASE
CYSTIC FIBROSIS
EDWARDS SYNDROME
FAMILIAL ADENOMATOUS POLYPOSIS (FAP)
FRAGILE X SYNDROME
HEMOCHROMATOSIS
HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC)
KERATOCONUS
KLINEFELTER'S SYNDROME
MARFAN SYNDROME
MYOPATHY
NEURAL TUBE DEFECTS
PHENYLKETONURIA (PKU)
PORPHYRIA
RETINOBLASTOMA
SYNDACTYLY
THALASSEMIA
TURNER'S SYNDROME
WILSON'S DISEASE
WOLFF-PARKINSON-WHITE SYNDROME
CLEFT PALATE/CLEFT PALATE AND LIP
DOWN SYNDROME
EPIDERMOLYSIS BULLOSA
FAMILIAL MEDITERRANEAN FEVER
FANCONI'S SYNDROME
G6PD DEFICIENCY
HEMOPHILIA
HUNTINGTON'S DISEASE
hypertrophic CARDIOMYOPATHY
LONG QT SYNDROME (LQTS)
MUSCULAR DYSTROPHY
myotonia congenita
PATAU SYNDROME
POLYDACTYLY
PROGERIA
SICKLE CELL DISEASE
TAY-SACHS DISEASE
TRIPLE X SYNDROME
VACTERL
VON WILLEBRAND'S DISEASE

Researchers have identified more than 6,000 monogenic (single gene) mutations that result in health disorders, affecting 1 child in every 200 born. Among them are CYSTIC FIBROSIS, SICKLE CELL DISEASE, MARFAN SYNDROME, HUNTINGTON'S DISEASE, and HEMOCHROMATOSIS. Other disorders, such as CLEFT PALATE/CLEFT PALATE AND LIP, result from polygenic (multiple gene) mutations or CHROMOSOMAL

DISORDERS, such as DOWN SYNDROME. Though as yet there are few treatments to alter the course of genetic and chromosomal disorders, continuing research holds promise that doctors may in the foreseeable future have the ability to offer effective therapeutic interventions.

Traditions in Medical History

In the 1660s English scientist Robert Hooke (1635–1703) used his newest invention, the compound light microscope, to examine a thin slice of cork. The increased magnifying power of this new microscope's dual lenses was considerable compared to the standard single-lens microscope of the time; and with its improved light source of reflected and focused candlelight, it revealed a level of structure in living organisms scientists had not known existed: the tight clustering of tiny compartments. Hooke called these compartments cells because they reminded him of the living quarters of monks in monasteries. Hooke described his findings and explorations of cells in his 1665 manuscript *Micrografia,* which became an epochal publication in the field of biology during Hooke's lifetime—short order for such significant recognition.

Not for another 150 years, however, did biologists finally and fully comprehend the interrelationships and organizations of cells within organisms. British botanist Robert Brown (1773–1858) discovered the cell nucleus in 1831, establishing it as the foundation of cell division; 36 years later Swiss biologist and chemist (Johann) Friedrich Miescher (1844–1895) isolated and identified the active protein–acid structure in the cell nucleus responsible for cell division. Miescher called the structure nuclein, and speculated that it not only was the key player in cell reproduction but also was the decanter of heredity itself. Miescher would never know the prophecy of his speculation because the technology to further explore such a hypothesis was still three quarters of a century away.

The words might well have gone from the scientist's mouth to the monk's ear, however. Merely a country's border away Gregor Johann Mendel (1822–1884) spent his days nurturing sweet peas in his monastery's gardens. Mendel, an Augustinian monk, observed in nature what Miescher studied in the laboratory: the paths of heredity. Mendel crossbred his sweet peas, detailing the patterns of their varieties and alternate characteristics. Mendel would later achieve full recognition for identifying the predictable variations that occurred as the consequence of what he called paired elements of heredity. Less than two years apart these two researchers, the chemist and the botanist, published their respective findings.

In 1933 Thomas Hunt Morgan (1866–1945) received the Nobel Prize in Physiology or Medicine for proving the existence of chromosomes. By the 1940s numerous scientists were trying to unravel the cryptogram of the chromosome. James Watson and Francis Crick, working in collaboration, and Maurice Wilkins, working independently, finally succeeded. In 1953 Watson and Crick unveiled their model of the double-helix structure of deoxyribonucleic acid. DNA, the master code of genetics, was no longer a secret. Watson, Crick, and Wilkins received the 1962 Nobel Prize in Physiology or Medicine "For their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material."

Increasingly sophisticated technology made it possible to study the activity of the cell at the level of the molecule. Following numerous affirming discoveries about genes and DNA sequencing in the 1960s, 1970s, and 1980s, scientists began to talk of sequencing the human genome—unraveling the molecule of heredity. The effort began formally in 1988 with James Watson at the helm of the planning process. Watson saw the Human Genome Project through its official launch in 1990. Only 13 years later, 2 years ahead of schedule and on the 50th anniversary of Watson and Crick's unveiling of the double helix, the Human Genome Project announced completion of the sequencing of the human genome. "Never would I have dreamed in 1953 that my scientific life would encompass the path from DNA's double helix to the three billion steps of the human genome," Watson said in comments to the media at the events celebrating the completion of the Human Genome Project.

Breakthrough Research and Treatment Advances

The high-tech world of genetics and molecular medicine continues to drive the direction of medicine. RECOMBINANT DNA technology debuted in the

1970s, representing a breakthrough in the ability to manipulate synthetic substances such as INSULIN to create products biologically identical to endogenous substances and launching what has become known as the biotech industry. Pharmacogenomics expands the intersection of genetics and pharmacology, with researchers in both disciplines developing customized medications that integrate with an individual's genotype to produce predictable, reliable, and effective results with minimal potential for adverse DRUG reactions. Many researchers believe aging itself is a function of genetics. Continued work to understand the details of the human genome makes it not only conceivable but likely that on the horizon are therapies to correct genetic mutations and chromosomal errors, and perhaps to overcome the dimensions of aging, that are deleterious to health.

Genetics and molecular medicine open new vistas in medical ethics as well. The line between life-altering treatments and altering life itself becomes increasingly blurred. GENETIC TESTING has the capability to tell not only what is already wrong with a person but what will go wrong in the future, and sometimes even with a timeline. Medical ethicists worry that such information is too much to know and that the risk is high for physicians and their patients (and other parties that have access to the information) to believe the book of life, as it were, is carved in stone rather than set in proteins. Many variables still remain within the control of individuals in regard to health and medical decisions. Environmental interactions—lifestyle factors—can modify most health conditions associated with genetic alterations. Even with all the knowledge arising from the science fiction–like world of genetics and molecular medicine, for many people lifestyle remains the critical turning point between health and disease.

A

allele Any of the variations of a GENE that may occupy the same position (locus) on a CHROMOSOME. The gene controlling a particular trait or function always occupies the same locus on the same chromosome. Genes occur as pairs, with one gene coming from each parent. The pairing determines how the gene's traits are expressed in the individual. For example, the gene for BLOOD TYPE occurs at region 34 on the long arm of chromosome 9, indicated as 9q34. This gene has three alleles, identified as 9q34IA, 9q34IB, and 9q34i (which geneticists sometimes abbreviate as IA, IB, and i, respectively). These alleles can occur in one of six pairings to produce the blood type A, B, O, or AB.

When the two alleles at the same locus are the same the individual is said to be homozygous for that gene; when the alleles are different the individual is heterozygous. In a heterozygous individual generally one allele is dominant and the other recessive. Occasionally each allele in a pairing has equal dominance, a circumstance called codominance. The 9q34i allele (type O) is recessive; the 9q34IA and 9q34IB alleles (type A and type B) are dominant. When the 9q34IA and 9q34IB alleles pair, their expression is codominant. The possible allele pairings for blood type can produce any of these expressions.

For further discussion of alleles within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also GENOTYPE; INHERITANCE PATTERNS; PHENOTYPE.

apoptosis The natural mechanism through which a cell engages in actions that lead to its death, often called programmed cell death or cell suicide. Apoptosis appears linked to SENESCENCE, an inherent limitation on the number of times a cell can divide. Both apoptosis and senescence play significant roles in the aging process. Once the cell initiates apoptosis there is no reversal; the process proceeds until the cell dies.

Apoptosis begins when the cell's DNA fragments, signaling or switching the rest of the process in motion. Once activated apoptosis sets in motion the subsequent events result in the cell's disman-

EXAMPLE ALLELE PAIRINGS AND EXPRESSION: BLOOD TYPE

Allele Pairing	Expression	Blood Type
IaIa (A+A)	Homozygous dominant	Type A
Iai (A+O)	Heterozygous dominant	
IbIb (B+B)	Homozygous dominant	Type B
Ibi (B+O)	Heterozygous dominant	
ii (O+O)	Homozygous recessive	Type O
IaIb (A+B)	Heterozygous codominant	Type AB

tling, assimilation, and recycling. In some respects cells become endlessly renewable resources for the body. Specialized cells called phagocytes break down dying and dead cells into basic components such as amino acids that other the body can use to construct new cells.

Apoptosis is necessary for growth, development, and change in the body. The process of the death of cells that experience injury or damage is called necrosis and by definition occurs outside the natural order of cell life expectancy. Extrinsic, rather than intrinsic, factors initiate necrosis.

See also CELL STRUCTURE AND FUNCTION; METABOLISM; PHAGOCYTE; PHAGOCYTOSIS; STEM CELL.

autosomal trisomy A chromosomal disorder in which there are three instead of the normal two copies of an AUTOSOME (nonsex chromosome). An autosomal trisomy may be complete (affect all cells) or mosaic (affect only some cells). The most commonly occurring complete autosomal trisomies that are survivable are those involving chromosomes 21, 18, and 13, which result in the chromosomal disorders DOWN SYNDROME (trisomy 21), EDWARDS SYNDROME (trisomy 18), and PATAU'S SYNDROME (trisomy 13). These trisomy disorders may also occur as a mosaic. Mosaic autosomal trisomies typically produce less severe, though still significant, physical and mental impairments. Complete autosomal trisomies affecting other chromosomes are often lethal, nearly always causing death early in development and well before birth.

Though the risk for autosomal trisomy disorders increases with a woman's age at the time she becomes pregnant, most autosomal trisomy disorders occur in pregnancies in younger women because the rate of CONCEPTION is significantly higher among younger women. The risk is highest for women who have previously given birth to a child with a trisomy disorder. Obstetricians can detect fetal trisomy disorders generally within the first and early part of the second trimesters of PREGNANCY with prenatal tests. The diagnostic path usually incorporates a combination procedures including

- BLOOD tests that look at the levels of proteins the FETUS and placenta are making
- ULTRASOUND, which shows physical anomalies that suggest a chromosomal disorder
- CHORIONIC VILLI SAMPLING (CVS) and AMNIOCENTESIS, which permit examination of fetal cells

See also BIRTH DEFECTS; CHROMOSOMAL DISORDERS; CONGENITAL ANOMALY; GENETIC COUNSELING; GENETIC TESTING; MOSAICISM; PREGNANCY.

autosome A CHROMOSOME that appears as a pair in which both chromosomes are the same in either sex, also called a nonsex chromosome. In contrast, the sex chromosomes appear as a pair that is different in males and females. The human GENOME contains 22 autosomes and one pair of sex chromosomes for a total complement of 46 chromosomes as 23 pairs.

For further discussion of autosomes within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also GENE; GENOTYPE; KARYOTYPE; PHENOTYPE; SEX CHROMOSOME.

C

cell structure and function The cell is the basic structural and functional unit of all living organisms. About 100 trillion cells make up one of the most complex of such organisms, the human.

Types of Cells in the Human Body

There are three basic types of cells in the body: stem cells, germ cells, and somatic cells.

The foundation of life: stem cells Stem cells are the primal, undifferentiated cells that give rise to all other cells. They are primarily abundant and functional during early embryonic development (embryonic stem cells). These are the cells of the blastocyst, the earliest form of a new life, and at this stage are totipotent: They have the ability to become any other kind of cell. Genes instruct dividing stem cells how to differentiate or form specific kinds of cells that then develop into various organs and body structures.

UMBILICAL CORD BLOOD STEM CELLS

The BLOOD that remains in the UMBILICAL CORD and PLACENTA at birth is an abundant source of multipotent BLOOD STEM CELLS. Cord blood transplantation is an emerging treatment for LEUKEMIA and other cancers as well as SICKLE CELL DISEASE and other blood disorders. Many people now opt to collect and store or donate the cord blood of their newborns after birth.

As the body takes shape stem cells become increasingly diffuse and specialized, transitioning to pluripotent (able to become cells of distinct body systems such as cardiovascular or gastrointestinal) and finally multipotent (able to become cells of specific kinds, such as BLOOD or BONE). The most versatile stem cell that remains when development is complete is the blood stem cell, which has the ability to differentiate into various types of blood cells throughout life. Other adult stem cells (also called somatic stem cells to distinguish them from embryonic stem cells) exist in most body tissues though are interspersed among other cells. Their role remains unclear though they appear responsible for large-scale regeneration of tissue such as can occur in the LIVER.

The cells of reproduction: germ cells Germ cells, also called gametes, are the cells of reproduction: the OVA or eggs (female) and the spermatozoa or SPERM (male). Gametes are haploid cells; each GAMETE contains one-half the complement of chromosomes. When two gametes merge in CONCEPTION, the resulting ZYGOTE acquires the full complement of genetic material.

The cells of the functioning body: somatic cells All cells that are not stem cells or germ cells are somatic cells. Somatic cells make up more than 99 percent of the cells in the adult body. They are diploid cells; each somatic cell contains the full complement of chromosomes. Somatic cells make up the organs and structures of the body. They are the body's primary working units, responsible for carrying out the myriad functions of METABOLISM that support life. Though similar in structure and function, somatic cells are broadly diverse in their activities and specializations.

Cell Structure

Most cells have standard, key structural components in common. These include

- PLASMA membrane, the cell's outer wall made up of a protein layer and a lipid (fatty) layer, that separates the cell's contents from its external environment yet permits interaction between the cell and the external environment

- cytoskeleton, a dynamic construct of filaments and fibers that support the cell's shape and inner components
- cytoplasm, a watery fluid that suspends the inner structures of the cell, moves substances through the cell, and conducts electricity
- nucleus, the core of the cell, separated from the cytoplasm by a thin membrane called the nuclear envelope, which contains the cell's chromosomes and genetic material
- mitochondria, self-replicating structures called organelles that generate the energy, in the form of adenosine triphosphate (ATP), the cell needs to function
- ribosomes, another type of organelle, which synthesize proteins according to genetic directions the mitochondrial RNA brings to the ribosomes
- lysosomes and peroxisomes, also organelles, which contain enzymes to break down cellular wastes into component molecules the cell can recycle

Cell Function

The cell is responsible for all of the functions of metabolism that support the body. Most of the body's 100 trillion cells have specialized responsibilities. Blood cells transport oxygen, GLUCOSE, and other NUTRIENTS throughout the body and collect molecules of metabolic waste that cells in the liver and KIDNEYS dismantle, recycle, or eliminate from the body. NERVE cells conduct electrical impulses. MUSCLE cells contract the HEART and move the body. Other cells make hormones, absorb nutrients, fight INFECTION, and so on. Regardless of their specializations, however, the primary activity of all cells is the synthesis of the enzymes and proteins that carry out the biochemical tasks of living.

Cell Division

One of the most important functions of a cell is to replicate itself, as this is the activity that sustains life. Some cells, such as those that line the gastrointestinal tract, replicate every 12 hours. Other cells, such as those in the heart and the liver, divide perhaps once every 12 months or so. Though cells have vast ability to perpetrate themselves in such fashion, there appear to be gene-mediated limits to the number of times cells may divide.

Cells replicate by dividing themselves, a process called mitosis (somatic cells) or meiosis (gametes). Mitosis is a multistage process during which the cell's chromosomes pull together and duplicate themselves. When this duplication is complete the cell then pulls apart into two new cells, called daughter cells, with one package of chromosomal content (called a CHROMATID) going with each daughter cell. In this way each daughter cell receives the full complement of chromosomes. Meiosis has two stages, meiosis 1 and meiosis 2. There is duplication of chromosomal material in meiosis 1 but not in meiosis 2, such that one cell ultimately produces four gametes.

For further discussion of cell structure and function within the context of genetics, please see the overview section "Genetics and Molecular Medicine."

See also APOPTOSIS; BLOOD TRANSFUSION; CENTROMERE; CHROMOSOME; HORMONE; INHERITANCE PATTERNS; PREGNANCY; SENESCENCE; SOMATIC CELL; STEM CELL; TELOMERE.

centromere The position on a CHROMOSOME where the chromosome separates during cell division. The centromere is a structure of noncoding DNA (DNA that does not convey genetic information). When the cell divides the strands of the chromatids migrate in opposite directions (pull apart) at the centromere. In a photomicrograph, the centromere appears as an indented, waistlike area on the chromosome. Geneticists use the centromere's position, along with other characteristics of the chromosome, to match chromosomes into their pairs when creating KARYOTYPES.

For further discussion of centromeres within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also ALLELE; CELL STRUCTURE AND FUNCTION; CHROMATID; GAMETE; GENE; GENOTYPE; PHENOTYPE; SOMATIC CELL; TELOMERE.

chromatid A replica of a CHROMOSOME that develops in preparation for cell division. Chromatids are "sister" pairs of each chromosome that contain identical genetic material. They remain

attached to each other at the CENTROMERE until cell division. When the mother cell divides, the sister chromatids separate at the centromere and migrate into the new daughter cells, forming the chromosome pairs for the new cells. Though minor variations are normal and frequently occur without causing problems because they affect relatively few cells, errors in chromatid replication and separation affect many or all cells and can be responsible for CHROMOSOMAL DISORDERS such as DOWN SYNDROME.

For further discussion of chromatids within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CELL STRUCTURE AND FUNCTION; DNA; GENETIC DISORDERS; MOSAICISM; MUTATION; NUCLEOTIDE; VARIATION.

chromosomal disorders Abnormalities affecting the chromosomes that result in syndromes (constellations of symptoms) having characteristic physical or functional anomalies. Most chromosomal disorders occur because of alterations in the number of chromosomes or the structure of chromosomes. Though an individual may inherit a chromosomal disorder, more commonly chromosomal disorders represent random occurrences. Typically all the cells in the body reflect the abnormality. Occasionally some but not all cells carry the chromosomal abnormality; this is a mosaic chromosomal disorder. A mosaic presentation tends to be milder than that observed when all cells carry the chromosomal abnormality

Disorders of Replication

Normally chromosomes exist in pairs. Replication errors can result in an incorrect number of chromosomes passing to new cells. Though such errors can occur in any cell with any episode of cell division, they are most harmful when they affect gametes (the sex cells, the ovum in the female and the spermatozoon in the male). Replication errors in gametes become chromosomal disorders in the new life created through their union. These errors may take the form of trisomy (an extra CHROMOSOME), monosomy (a missing chromosome), or uniparental disomy (both copies of a chromosome come from the same GAMETE or parent).

Trisomy Disorders of trisomy occurs when the ZYGOTE receives three instead of the normal two copies of a chromosome. Most trisomies are autosomal, and most autosomal trisomies are lethal very early in embryonic development. Most early losses due to trisomy thus likely escape detection. The survivable autosomal trisomies affect chromosome 13 (PATAU'S SYNDROME), chromosome 18 (EDWARDS SYNDROME), and chromosome 21 (DOWN SYNDROME). Trisomies can also involve the sex chromosomes. The most common such disorder is KLINEFELTER'S SYNDROME, in which the zygote receives two (and sometimes more) X chromosomes and one Y chromosome. Though the Y chromosome determines the gender as male, the additional X chromosome affects sexual development and FERTILITY. The zygote may also receive three X chromosomes (triple X syndrome) or one X chromosome and two Y chromosomes. These trisomies may not produce obvious symptoms, though often boys who have XYY syndrome have developmental delays and learning disabilities.

Monosomy Monosomy occurs when the zygote receives only one copy of a chromosome and overall occur far less frequently than trisomy because an entire missing autosome (nonsex chromosome) is nearly always lethal. The monosomy disorder Turner syndrome, in which the zygote receives only one X SEX CHROMOSOME, is one of the few survivable monosomy disorders. Because the single sex chromosome is X, the zygote is female although breast development at sexual maturity is diminished.

Uniparental disomy In uniparental disomy the zygote receives two copies of a chromosome from one gamete and none from the other gamete. Though in many cases this REPLICATION ERROR may result in no adverse symptoms or consequences, it can allow rare recessive disorders to manifest. Uniparental disomy also causes symptoms when the involved chromosome is one in which GENETIC IMPRINTING is essential. In such circumstances the chromosome pairing requires one chromosome from each parent to activate the chromosome's genetic functions.

Disorders of Structure

Chromosomal disorders of structure occur when there are physical changes to the chromosome

that alter its configuration. In TRANSLOCATION, fragments of a chromosome break away and reattach to other chromosomes or are lost, potentially changing several chromosomes with unpredictable and random results. Inversions, rings, duplications, and deletions are other disorders of structure involving fragments of the chromosome that are fairly uncommon though tend to produce symptoms when they occur. The types of symptoms depend on the involved chromosome.

Inversions In a chromosomal inversion the chromosome breaks in two or more locations, then the segments rejoin with one or more segments inverted (upside-down). Some genetic material may be lost in the process, and the genes are out of position. Inversions may or may not cause symptoms, depending on the involved chromosome and the degree of inversion.

Rings Chromosomal rings occur when the ends of the chromosome are missing and the remaining chromosome reshapes itself into a ring. The extent and nature of symptoms depends on the involved chromosome and the amount of missing genetic material. A ring of chromosome 15, for example, tends to produce symptoms such as facial anomalies and growth deficiency.

Duplications and deletions In duplications and deletions, the chromosome acquires (duplication) or loses (deletion) fragments of its structure. The severity of the consequences depends on the chromosome involved and the extent of the altered genetic material.

Symptoms and Diagnostic Path

The symptoms of chromosomal disorders vary with the chromosome involved and the extent of damage present. Because chromosomal disorders tend to affect large segments of genetic material, the resulting symptoms and syndromes are often complex and affect multiple organs, structures, functions, and systems. The diagnostic path may include imaging procedures such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI) to evaluate structural anomalies of internal organs. A KARYOTYPE (picture of the chromosomes a in a cell) reveals overt chromosomal problems, and molecular studies may be necessary to unravel the circumstances of less obvious chromosomal disruptions.

Treatment Options and Outlook

For nearly all chromosomal disorders, treatment focuses on improving physical anomalies and maintaining function to the extent possible. Children born with chromosomal disorders often require ongoing medical care and other kinds of support. Outlook and QUALITY OF LIFE vary widely even within the same syndrome.

Risk Factors and Preventive Measures

Most chromosomal disorders are random events for which there are no preventive measures. Parental age and exposure to teratogenic substances (chemicals, drugs, or other materials that disrupt embryonic or fetal development) are risk factors for certain chromosomal disorders. Doctors recommend all women of childbearing age who could become pregnant, whether or not they are planning PREGNANCY, take folic acid supplementation, which appears to reduce the risk for numerous congenital anomalies and perhaps chromosomal damage.

See also CONGENITAL ANOMALY; GENETIC DISORDERS; INHERITANCE PATTERNS.

chromosome A coiled DNA molecule within the cell's nucleus that carries an individual's GENETIC CODE. Most of the time the chromosome's structure is loose and indistinguishable. Only in the stage of cell division immediately before the cell divides (the metaphase) does the chromosome draw itself into a compact, rodlike structure the geneticist can see under a microscope after applying a special dye to the cell that the chromosomes absorb. It is this ability to absorb a colored dye that gives the chromosome its name, which means "colored body."

Chromosome Complements

The nucleus of every diploid cell, also called a SOMATIC CELL, contains the full complement of 46 chromosomes arranged in 23 pairs. One pair contains the sex chromosomes that establish gender, paired either as XX (female) or XY (male). The other 22 pairs are autosomes. The haploid cells, the gametes (spermatozoa and OVA), contain one half the chromosome complement. When gametes merge in CONCEPTION the diploid cell they form, the ZYGOTE, acquires the full chromosomal comple-

ment. The only cells in the body that do not have chromosomes are the erythrocytes, which do not have nuclei.

Autosomes carry the bulk of genetic code. Thousands of genes line each autosome, each in its ordained position. The sex chromosomes carry several hundred genes. The GENE positions, called loci (in the singular, each position is a locus), are constant. For example, the gene loci for the ABO BLOOD TYPE are always on chromosome 9, those for the rhesus (Rh) blood type are on chromosome 1, and those for EYE color on chromosomes 15 and 19.

CHROMOSOME SIZE

The HUMAN GENOME PROJECT, completed in 2003, revealed the structure of chromosomes to be much larger and more complex than scientists previously had theorized. Chromosome 1, the largest CHROMOSOME, contains 2,968 genes. The smallest chromosome, the Y chromosome, contains 231 genes.

Nomenclature

Geneticists designate the normal female chromosome complement as 46,XX and the normal male chromosome complement as 46,XY. Deviations from the norm are CHROMOSOMAL DISORDERS geneticists designate according to the deviation, for example 47,XY,+21 denotes AUTOSOMAL TRISOMY 21 (DOWN SYNDROME) in a male. The designation 45,X denotes TURNER SYNDROME, a monosomy disorder (missing chromosome) affecting the SEX CHROMOSOME in a female. A comprehensive standard of nomenclature (naming) exists so all geneticists can use a common "language" when describing chromosomal and genetic configurations.

A chromosome's structure consists of two telomeres (end segments), a CENTROMERE (waistlike indentation), and two arms (the segments above and below the centromere). The centromere is somewhat off-center, such that each chromosome has a short arm (designated "p" for *petite*) and a long arm (designated "q" because scientific nomenclature is alphabetical). The regions of each arm are numbered. Geneticists identify a gene's locus relative to its placement on the chromosome. The gene responsible for CYSTIC FIBROSIS, for example, is identified as CFTR 7q31.2—cystic fibrosis transmembrane conductance regulator located in band 31, region 2, on the long arm of chromosome 7.

For further discussion of chromosomes within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also AUTOSOME; ERYTHROCYTE; GAMETE; GENETIC DISORDERS; GENOME; GENOTYPE; PHENOTYPE; SPERM; TELOMERE.

cloning The creation of exact copies of a GENE, cell, or entire organism. Such exact copies occur naturally when a ZYGOTE divides to become identical multiples such as twins or, less commonly, triplets. Manipulated cloning is primarily a research method at present, though scientists use cloning for therapeutic applications in creating RECOMBINANT DNA products such as INSULIN. Insulin was the first human gene cloned (1978) as well as the first genetically engineered product approved for use in the United States (1982). The cloning of entire organisms, such as Dolly the sheep in 1997, though sensational, is extraordinarily challenging. Currently, cloned organisms appear prone to numerous health problems and tend to die prematurely, which somewhat mystifies researchers because natural clones such as identical twins do not experience these challenges. Numerous ethical issues surround the use of entire organism cloning, particularly EMBRYO cloning.

Scientists create gene clones by removing the DNA from a vector such as a bacterium cell and replacing it with the DNA of choice. The bacterium rapidly replicates, creating multiple identical copies of the DNA. Similarly, this process can create identical replicas of cells. Researchers are hopeful that this technology will someday lead to the ability to generate replacement tissues and organs to treat various health conditions that currently rely on therapies such as ORGAN TRANSPLANTATION. This technology further holds promise for treating degenerative conditions such as PARKINSON'S DISEASE and HUNTINGTON'S DISEASE. Cloning is also one method of potential GENE THERAPY.

See also CELL STRUCTURE AND FUNCTION; ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE.

congenital anomaly A physical abnormality present at birth. Congenital anomalies, also called BIRTH DEFECTS, can affect nearly any structure in the body and may be hereditary or random. GENETIC DISORDERS and exposure to teratogens (substances, such as drugs, that alter the development of the embryo or fetus) account for the majority of congenital anomalies. The symptom constellations that characterize CHROMOSOMAL DISORDERS typically contain multiple congenital anomalies.

Some congenital anomalies are almost always treatable, such as atrial septal defect (an abnormal opening in the septum, or wall, between the two atria in the HEART) or CLEFT PALATE/CLEFT PALATE AND LIP (failure of the oral structures to properly close). Other congenital anomalies are life-altering or life-threatening, such as severe forms of SPINA BIFIDA (in which the spine fails to form properly) or transposition of the great arteries (incorrect alignment of the major BLOOD vessels in the heart).

Many congenital anomalies are physically apparent at birth or manifest symptoms that reveal their presence. An infant born with congenital anomalies of the heart, for example, may have a bluish hue to the SKIN (CYANOSIS) that indicates insufficient oxygen to the tissues. The diagnostic path may include imaging procedures such as ULTRASOUND, COMPUTED TOMOGRAPHY (CT) SCAN, and MAGNETIC RESONANCE IMAGING (MRI) that allow the neonatologist to visualize and identify the anomaly. GENETIC TESTING may also be appropriate, depending on the nature of the anomaly. Treatment depends on the type, extensiveness, and complexity of the anomaly. Surgeons often can easily repair isolated anomalies, such as cleft lip or atrial septal defect, with minimal or no residual consequences. Extensive or multisystem anomalies may not be treatable.

See also CONGENITAL HEART DISEASE; HORSESHOE KIDNEY; REPLICATION ERROR.

cystic fibrosis An inherited genetic disorder resulting from multiple mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) GENE on CHROMOSOME 7, inherited as autosomal recessive mutations. Researchers believe as many as 10 million people may be cystic fibrosis carriers and unaware of it. Though researchers know of approximately 600 CFTR mutations, one MUTATION, called the delta F508 mutation, accounts for about 70 percent of cystic fibrosis in the United States. About 30,000 Americans live with cystic fibrosis.

CFTR is a protein that, when functioning normally, facilitates the transport of chloride and other ions across cell membranes. In cystic fibrosis the presence of CFTR is greatly diminished and salts fail to properly cross the cell membranes. One result is very high concentrations of salts in the sweat, particularly chloride, giving the SKIN a salty taste. The effect of diminished CFTR is most pronounced on epithelial secretory cells—the cells that form mucous membranes and make up the linings of the intestinal tract, LUNGS, and urinary system, which rely on sodium chloride and other salts to draw fluid into their secretions. Without CFTR the normal watery secretions of these cells become thick and sticky.

Cystic fibrosis most seriously affects the pulmonary and gastrointestinal systems, and does so in all people who have the disorder, though the disorder involves all body systems to varying extents. Thickened secretions accumulate in the airways in the lungs, creating obstructions that interfere with BREATHING as well as establish breeding grounds for BACTERIA and other pathogens. Furthermore, the high chloride content on the surface of the epithelial cells that line the bronchial structures suppresses the body's natural bacterial-control mechanisms. People who have cystic fibrosis have frequent or chronic upper respiratory infections and pneumonias. About 85 percent of people who have cystic fibrosis also develop pancreatic insufficiency, in which the DIGESTIVE ENZYMES the PANCREAS normally secretes do not adequately support digestion.

Symptoms and Diagnostic Path

Infants who have cystic fibrosis may have MECONIUM ileus at birth, an obstruction of the bowel with meconium, a tarry substance that normally passes from the RECTUM within a few hours of birth. Other signs and symptoms of cystic fibrosis may emerge at any time and include

- large, foul-smelling, greasy-looking stools
- frequent bowel blockages

- thick SPUTUM
- coughing and wheezing
- clubbing of the fingers and toes
- INTUSSUSCEPTION (a segment of the bowel "telescopes" into another segment), a potentially life-threatening circumstance
- RECTAL PROLAPSE
- nasal polyps

Men who have cystic fibrosis nearly always have congenital bilateral absence of the vas deferens, which results in INFERTILITY, though the TESTES and other structures of the male sex organs function normally.

The diagnostic path begins with a skin salt test that measures the amount of chloride present on the surface of the skin. In cystic fibrosis these levels are five to six times normal; such a finding is generally conclusive of a diagnosis of cystic fibrosis, especially in combination with other characteristic symptoms. A BLOOD or saliva test also can confirm the presence of a cystic fibrosis mutation. Other blood tests help to assess the level of damage organ systems have experienced.

Treatment Options and Outlook

The most serious and common consequence of cystic fibrosis is lung damage. Doctors may prescribe ANTIBIOTIC MEDICATIONS to curtail infections, mucolytic agents and mechanical methods such as CHEST PERCUSSION AND POSTURAL DRAINAGE to help thin secretions, and bronchodilator medications to open the airways. An aerosol spray medication, dornase alpha, uses enzymes to break up secretions so the person can more easily COUGH them up. Other treatments may include pancreatic enzyme supplementation and high liquid consumption.

Cystic fibrosis is the leading reason for LUNG TRANSPLANTATION, which is a treatment that becomes necessary when the lungs can no longer function. Some people who have severe cystic fibrosis undergo simultaneous pancreas and lung transplantation. Such surgery is extensive and ORGAN TRANSPLANTATION requires lifelong IMMUNOSUPPRESSIVE THERAPY. These treatments are relatively new, so doctors do not know their long-term success. With appropriate medical management some people who have cystic fibrosis can live into at least midlife with relatively few significant complications.

Risk Factors and Preventive Measures

Cystic fibrosis is an autosomal recessive disorder acquired when each parent carries the gene mutation. Preconception GENETIC SCREENING is the only way to prevent parents from passing cystic fibrosis to their children. Because the projected number of cystic fibrosis carriers is so high (1 in 20 among Caucasians of northern European ancestry), many doctors offer cystic fibrosis screening to adults who are planning families. Though researchers hope GENE THERAPY may offer a cure for cystic fibrosis in the future, such approaches are only in the early stages of experimentation.

See also CARRIER; CYSTIC FIBROSIS AND THE LUNGS; FAMILY PLANNING; GENETIC COUNSELING; GENETIC DISORDERS; INFECTION; INHERITANCE PATTERNS; NASAL POLYP; PATHOGEN; PNEUMONIA.

D

DNA The abbreviation for deoxyribonucleic acid. DNA is the molecule of heredity; its sequences form the body's GENETIC CODE. Each cell in the body contains DNA within the chromosomes in its nucleus (except erythrocytes, which do not have nuclei). DNA has a characteristic double-helix structure that resembles a gently twisting ladder. The supporting rails of this structure are deoxyribose, a sugar-phosphate, and the cross-bands are nitrogen bases: adenine (A), thymine (T), guanine (G), and cytosine (C). These bases pair in precise, predictable patterns arranged in nearly endless combinations, more than three billion in all.

British scientists James Watson and Francis Crick unraveled the double-helix structure of DNA in 1953, identifying its two spiraling, sugar–phosphate (deoxyribose) supports and cross-bands of paired nucleic acids. Just 50 years later researchers involved with the HUMAN GENOME PROJECT concluded their mapping of the human GENOME, which included determining the entire biochemical sequence of human DNA. Chromosomes are structures of DNA, and genes are segments of chromosomes (also made up of DNA).

For further discussion of DNA within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CELL STRUCTURE AND FUNCTION; CHROMOSOME; ERYTHROCYTE; GENOTYPE; RNA.

Down syndrome An AUTOSOMAL TRISOMY disorder that results from a REPLICATION ERROR during cell division in which a GAMETE (sex cell) ends up with two copies of CHROMOSOME 21 instead of the normal single copy (as haploid cells, gametes contain one half the complement of chromosomes). At CONCEPTION the ZYGOTE thus ends up with three instead of the normal two copies of chromosome 21, which ultimately produces multiple congenital anomalies. When all cells carry the extra chromosome, the resulting anomalies occasionally may be so severe that the disorder is lethal before birth. Sometimes Down syndrome occurs as a mosaic disorder in which some but not all cells contain the extra chromosome 21, which typically produces milder symptoms.

Down syndrome occurs in about 1 in 1,200 live births in the United States and about 350,000 Americans currently live with Down syndrome, many independently. Though the risk for Down syndrome increases dramatically with maternal age, most infants who have Down syndrome are born to younger mothers because the increased rate of CONCEPTION more than offsets the increase in age-related risk. Down syndrome is the most commonly occurring of the autosomal trisomy disorders.

Symptoms and Diagnostic Path

Children born with Down syndrome often have characteristic facial features, which include

- flat, upwardly slanting eyes with extra fatty tissue in the lids
- rounded face with a small NOSE and MOUTH
- small ears
- broad, short neck
- short stature with noticeably small hands and short fingers

Other findings of Down syndrome include congenital anomalies affecting the HEART, intestines, and other organs. About half of infants born with

Down syndrome have atrial or ventricular septal defects (openings or holes in the septum, or wall, between the chambers of the heart). About half also have impaired vision (notably, congenital cataracts and AMBLYOPIA) and partial to complete HEARING LOSS. About 10 percent have malformations of the intestines that require surgical correction. All individuals with Down syndrome have some intellectual impairment. Mild to moderate intellectual impairment is most common. Some children who have Down syndrome do well in regular classes in school and grow up to be capable of independent living.

Doctors often can diagnose Down syndrome and other autosomal trisomy disorders before birth using prenatal screening methods such as blood tests, ULTRASOUND, AMNIOCENTESIS, and CHORIONIC VILLI SAMPLING (CVS). These methods retrieve cells from the FETUS from which a geneticist can construct a KARYOTYPE, which presents photomicrographic images of the fetus's or infant's chromosomes. Advanced maternal age (mother's age over 40) and the previous conception of a child with Down syndrome or another autosomal trisomy disorder are the leading risks for Down syndrome. Whether done prenatally or after birth the karyotype provides definitive diagnosis.

Treatment Options and Outlook

There are no specific treatments for Down syndrome. Because children who have Down syndrome are more susceptible to INFECTION, they often need more medical care while growing up. There is a high correlation between early-onset ALZHEIMER'S DISEASE and adults who have Down syndrome. Typically men who have Down syndrome are sterile, though women who have Down syndrome may be fertile and can become pregnant. Their risk for conceiving a child with Down syndrome is very high, however, and doctors strongly recommend GENETIC COUNSELING.

About 350,000 Americans live with Down syndrome. Because Down syndrome is the mildest of the survivable trisomy disorders and because it can occur in a mosaic rather than a complete presentation, some people who have it are able to lead relatively independent and productive lives, living into their mid-50s or beyond. Early treatment for the anomalies common with Down syndrome, such as septal defects, and ongoing care for other health conditions, such as HYPOTHYROIDISM and VISION IMPAIRMENT, have greatly improved both health and QUALITY OF LIFE for people who have Down syndrome.

Risk Factors and Preventive Measures

Down syndrome occurs as a replication error that does not appear to be preventable, though recent research suggests that folic acid supplementation beginning before conception and extending through PREGNANCY, such as obstetricians recommend for preventing NEURAL TUBE DEFECTS, may reduce the risk for Down syndrome. Older women, who have a higher risk of conceiving a child with Down syndrome, may opt for genetic testing early in pregnancy to determine whether the fetus has the trisomy 21 GENOTYPE. Knowing allows the woman to make appropriate plans and decisions regarding the pregnancy and potential care needs of the child.

CONGENITAL ANOMALIES CHARACTERISTIC OF DOWN SYNDROME

AMBLYOPIA	atrial septal defect
BOWEL ATRESIA	broad, short neck
congenital cataracts	developmental delays
flat, upwardly slanting eyes	HEARING LOSS
intellectual impairment	rounded face
short stature	small ears
small hands and short fingers	small NOSE and MOUTH
ventricular septal defect	

See also AUTOSOME; CATARACT; CONGENITAL ANOMALY; CHROMOSOME DISORDERS; CONGENITAL HEART DISEASE; EDWARDS SYNDROME; ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; GENETIC SCREENING; INHERITANCE PATTERNS; MOSAICISM; PATAU'S SYNDROME; PRENATAL CARE.

E–F

Edwards syndrome An AUTOSOMAL TRISOMY disorder that results from a REPLICATION ERROR during cell division in which a GAMETE (sex cell) ends up with two copies of CHROMOSOME 18 instead of the normal single copy (as haploid cells, gametes contain one half the complement of chromosomes). At fertilization the ZYGOTE thus ends up with three instead of the normal two copies of chromosome 18, which ultimately produces multiple and life-threatening congenital anomalies.

When all cells carry the extra chromosome 18), the anomalies are so severe that the defect often is lethal well before birth. Sometimes Edwards syndrome occurs as a mosaic trisomy disorder (some but not all cells contain the third chromosome 18), which tends to produce milder though nonetheless significant symptoms. Edwards syndrome occurs in about 1 in 5,000 live births in the United States, 80 percent of which are females. Researchers do not know whether Edwards syndrome affects females more often or if females are more likely to survive beyond birth.

Children born with Edwards syndrome have severe and complex physical deformities involving multiple organs and systems that require extensive medical care from the time of birth. Most also have profound intellectual impairment arising from malformations affecting the BRAIN and NERVOUS SYSTEM. A KARYOTYPE confirms the diagnosis. Fewer than 10 percent of infants born with Edwards syndrome survive the first year after birth; those who do require extensive, ongoing medical care and developmental support. Survival beyond five years is extremely rare.

Doctors often can diagnose Edwards syndrome and other autosomal trisomy disorders before birth, through prenatal screening methods such as AMNIOCENTESIS and CHORIONIC VILLI SAMPLING (CVS). These methods retrieve cells from the FETUS from which a geneticist can construct a karyotype. Advanced maternal age (mother's age over 40) and the previous CONCEPTION of a child with Edwards syndrome or another autosomal trisomy disorder are the leading risks for Edwards syndrome. Whether done prenatally or after birth the karyotype, which presents photomicrographic images of the fetus's or infant's chromosomes, provides definitive diagnosis.

CONGENITAL ANOMALIES CHARACTERISTIC OF EDWARDS SYNDROME

facial deformities
fingers curled over one another in clenched fists
heart defects
kidney abnormalities
low, small ears
microcephaly (small head and BRAIN)
small MOUTH and cleft deformities
spina bifida
SYNDACTYLY
TALI PEDES (club foot)

See also AUTOSOME; CHROMOSOME DISORDERS; CONGENITAL ANOMALY; CONGENITAL HEART DISEASE; DOWN SYNDROME; ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; GENETIC SCREENING; INHERITANCE PATTERNS; MOSAICISM; PATAU'S SYNDROME; PRENATAL CARE.

ethical issues in genetics and molecular medicine The questions and concerns that arise for physicians and individuals in regard to the information GENETIC SCREENING, GENETIC TESTING, and genetic and molecular therapies. Though advances in genetics have produced significant breakthroughs in understanding, diagnosing, and sometimes treating health conditions that occur as a result of GENETIC

DISORDERS, doctors and their patients grapple with the ethics of both research and therapeutics. The issues touch many of what have long been the sacred tenets of the practice of medicine: privacy, access to care, autonomy in decision making, and protection against discrimination.

Privacy

Most health conditions, with the exception of infectious diseases, affect only the individuals who have them. Matters of diagnosis, treatment, and prognosis remain private between physician and patient (and, some would add, third-party insurers). Genetic issues affect families, current and prospective. Doctors, especially family practitioners who care for multiple members of the same family, may find themselves in conflict in regard to genetic information about one family member that affects the health or health prospects of other family members.

Access to Care

Diagnostic and therapeutic applications of genetic technology are both complex and expensive. Many procedures are available only in research facilities or are not covered by conventional HEALTH INSURANCE plans. People who participate in clinical studies may have access to technologies that people who choose not to participate in research cannot have. As well, questions arise in regard to the relative value of certain applications of genetic technology. What purpose does genetic testing serve when there is no treatment or cure for the genetic condition? This is a particular issue for adults who may carry GENE mutations for genetic disorders such as HUNTINGTON'S DISEASE, for whom the disease is inevitable if they have the MUTATION but for which at present there is no means to mitigate symptoms or the disease's unpleasant progression, although promising therapies may be available soon. Some health experts argue that resources provide greater benefit for the larger good when they go toward conditions for which prevention, treatment, or cure is possible.

Informed and Autonomous Decision Making

For as much as researchers have learned and now know about human genetics there remain vast unknowns about the potential benefits, risks, and complications of genetically based treatments. In 2003 the US Food and Drug Administration (FDA), which oversees clinical research and approves new treatments, suspended certain GENE THERAPY methods after people receiving apparently successful results suddenly acquired lethal leukemias. Informed consent, long the mainstay of treatment decision making, is increasingly difficult to apply. Other ethical issues arise in regard to making decisions about genetic conditions that affect the lives and circumstances of children or other family members. Further concerns involve legal and forensic applications of genetic information.

Discrimination

As technology provides ever-expanding knowledge, concerns also grow that what people learn about their health status could end up being used against them in settings ranging from health and life insurance coverage to job offers and even medical care opportunities. Though such concerns are not new, the inevitabilities of certain genetic outcomes put discrimination concerns in new perspective.

For further discussion of medical ethics within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CLONING; LEUKEMIA; QUALITY OF LIFE.

familial Mediterranean fever An inherited genetic disorder that results in repeated episodes of arthritis (INFLAMMATION of the joints), PERITONITIS (inflammation of the membrane that lines the abdominal cavity), pleuritis (inflammation of the membrane that surrounds the LUNGS), and PERICARDITIS (inflammation of the membrane that contains the HEART). FEVER accompanies the outbreaks of inflammation, which occur without apparent precipitating factors and not in any particular pattern. In some people the disorder also includes AMYLOIDOSIS, in which deposits of amyloid (a waxlike substance) accumulate in organs such as the KIDNEYS.

Familial Mediterranean fever, as the name implies, occurs predominantly among people of Mediterranean descent and is an autosomal recessive disorder. The responsible mutated GENE is on the short arm of CHROMOSOME 16. At present there

are no genetic tests or diagnostic procedures that conclusively diagnose familial Mediterranean fever; the doctor makes the diagnosis on the basis of family history and the pattern of symptoms.

See also AUTOSOME; GENETIC DISORDERS; INHERITANCE PATTERNS; MUTATION; RENAL FAILURE.

family medical pedigree A comprehensive listing of relatives and their medical conditions, including information about diseases that may have genetic foundations. A family medical pedigree looks somewhat like a genealogic family tree, with branched lineage to show family relationships (such as marriage, birth, half-siblings). The family medical pedigree should extend at least three generations and list each person's age at the time of death, the cause of death, and any known history of diseases or symptoms.

Many of the health conditions doctors know today are genetic in origin were not known, either as diseases or as GENETIC DISORDERS, even one or two generations ago, so documenting symptoms can help reveal undetected genetic conditions. Maintaining a record of personal health symptoms and conditions, and similar information for children, can further provide important clues about genetic factors in health and in illness.

See also GENOME; INHERITANCE PATTERNS; MUTATION; PERSONAL HEALTH HISTORY.

fragile X syndrome An inherited genetic disorder that results in significant intellectual impairment. Fragile X syndrome arises from a monogenic (single-GENE), increased repeat MUTATION affecting the FMR1 gene on the X CHROMOSOME and is the leading cause of inherited intellectual impairment in males. Fragile X syndrome more severely affects males because females have a second X chromosome that can somewhat override the mutated gene on the other X chromosome. Most females are unaffected carriers. Because males have one X chromosome and one Y chromosome, they lack this dampening affect. A male can also be an unaffected CARRIER of the mutated gene, though this is very rare, and will thus pass the mutation to all of his daughters though none of his sons.

The symptoms of fragile X syndrome vary in severity though typically include

- developmental delays
- speech impairments
- intellectual impairment (sometimes profound)
- seizures
- behavioral problems
- AUTISM-like characteristics
- physical features that may include overly flexible joints, flat feet, long facial configuration, and oversized ears

Diagnosis occurs through GENETIC TESTING, typically cytogenic analysis. Treatment may include supportive measures such as special education in school, speech and language pathology, and medications to moderate behaviors and control seizures. Children who are mildly affected may require little extra care and may attend regular classes and schools; those who are severely affected may require ongoing support and institutional care.

See also DOWN SYNDROME; GENETIC COUNSELING; GENETIC DISORDERS; INHERITANCE PATTERNS; PHENYLKETONURIA (PKU); SEIZURE DISORDERS.

gamete A spermatozoon (SPERM cell) or an ovum (egg cell). A gamete, also called a germ cell or sex cell, is a haploid cell; it contains half the complement of chromosomes and genetic material necessary to encode (result in creating) an individual. When two gametes merge they produce a single diploid cell, the ZYGOTE, which then contains the full complement of chromosomes needed for life.

For further discussion of gametes within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CELL STRUCTURE AND FUNCTION; CHROMOSOME; CONCEPTION; OVULATION.

gene A segment of coding DNA (DNA that instructs the structure and function of cells throughout the body) composed of a specific sequence of nucleotides. The gene is the basic unit of inheritance that directs every facet of the body's appearance and functions. Genes align along chromosomes in pairs. Each CHROMOSOME (AUTOSOME) contains thousands of genes, except the sex chromosomes which contain only a few hundred genes.

Each gene has a specific location on the chromosome, called its locus, and encodes a specific function (either a protein or RNA transcription). The HUMAN GENOME PROJECT identified 19,599 confirmed genes and 2,188 probable genes at its conclusion in April 2003. GENETIC DISORDERS occur when there are disruptions of the ALLELE pairings or there is damage to the gene or the chromosome at or near the gene's locus.

Each gene has a specific task, which it carries out through a process called encoding. The gene instructs the cells to synthesize (produce) a specific protein. Ribosomes, specialized structures within each cell, synthesize the proteins. The protein then carries the gene's message to its target and initiates the appropriate sequence of biochemical events to implement the message.

For further discussion of genes within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CHROMOSOMAL DISORDERS; GENOME; INHERITANCE PATTERNS; MUTATION; NUCLEOTIDE; SEX CHROMOSOME.

gene therapy Treatment methods, most of which remain experimental, that attempt to manipulate genetic structure or gene encoding. GENE therapy targets either germline (GAMETE) or somatic cells, using vectors to deliver genes within cells. Germline gene therapy aims to prevent a genetic disorder from passing to new generations, while somatic gene therapy targets genetic disorders that already exist in individuals. Most often the goal of gene therapy is to replace a defective gene with a healthy, functional gene. The vectors typically used are inactivated viruses into which scientists insert the replacement gene. The VIRUS enters the target cell and delivers the gene.

Applications of gene therapy have not been as successful as researchers have hoped was possible, however, and at present the US Food and Drug Administration (FDA) has not approved any gene therapy methods for use in the United States. The effects of gene therapy appear time-limited, and viral vectors often initiate immune responses. Researchers continue to investigate safe and effective mechanisms to therapeutically manipulate genes with the goal of treating or curing GENETIC DISORDERS.

See also ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; MOLECULARLY TARGETED THERAPIES; RECOMBINANT DNA; SOMATIC CELL.

genetic carrier An individual whose GENOTYPE contains a recessive GENE MUTATION capable of causing a genetic disorder though the individual does not have or show symptoms of the disorder the mutation causes. Typically a genetic CARRIER has one "good" gene and one mutated gene. A genetic carrier may pass on the mutated gene to his or her biological children, though typically two mutated genes are necessary for the child to acquire the genetic disorder.

See also CELL FUNCTION AND STRUCTURE; GENETIC DISORDERS; GENETIC SCREENING; GENETIC TESTING; INHERITANCE PATTERNS.

genetic code The organizations of nucleotides (DNA sequences) within messenger RNA into triplet structures called trinucleotides or codons. The codons convey the order of amino acids for the structure of the protein for which a particular GENE encodes. The process of protein synthesis takes place in the ribosomes in the cell cytoplasm; the messenger RNA carries the encoding to the ribosomes.

See also CELL STRUCTURE AND FUNCTION; CHROMOSOME; GENOME; GENOTYPE; NUCLEOTIDE; PHENOTYPE.

genetic counseling A multidisciplinary approach to evaluating the risk for specific genetic diseases or CHROMOSOMAL DISORDERS. Doctors often recommend genetic counseling for people who have strong family history for GENETIC DISORDERS such as TAY-SACHS DISEASE or HUNTINGTON'S DISEASE and older women who are or who are planning to become pregnant. Obstetricians also will recommend genetic counseling for couples who receive positive results from prenatal genetic tests so they may make informed decisions and conduct appropriate planning for pregnancies in which there are genetic or chromosomal abnormalities.

A genetic counseling team may include a clinical geneticist (physician specializing in genetics and molecular medicine), genetic psychologist, and a social worker. The intent of genetic counseling is to evaluate family history, results of genetic tests, and current health circumstances to provide individuals, couples, or families with as much information as possible about whatever genetic risks or situations they are facing and the options for addressing them.

The role of the genetic counseling team is to answer questions and provide support for the decisions individuals and couples make. Major healthcare centers and high-risk obstetrical practice groups generally have genetic counseling practitioners and services available.

See also ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; FAMILY MEDICAL PEDIGREE; GENETIC SCREENING; GENETIC TESTING; PREGNANCY.

genetic disorders A collective classification for syndromes, diseases, and congenital anomalies that result from alterations of the genes and chromosomes. There are four general categories of genetic disorders, each relating to the way in which the alterations manifest.

Chromosomal Disorders

The normal human GENOME contains 23 paired chromosomes. CHROMOSOMAL DISORDERS occur when there are disruptions in these pairings in which there is an extra CHROMOSOME (trisomy) or a missing chromosome (monosomy). Chromosomal disorders also occur when large segments of a chromosome are damaged or missing (deletion syndromes). Less often, a broken segment of a chromosome attaches itself to another chromosome (TRANSLOCATION). Common chromosomal disorders include DOWN SYNDROME, EDWARDS SYNDROME, PATAU'S SYNDROME, TURNER SYNDROME, and KLINEFELTER'S SYNDROME.

Single-Gene Disorders

Each GENE encodes, or directs, a specific action within the body. Single-gene disorders, in which a MUTATION of a gene or set of genes causes malfunctions of the proteins that carry out the gene's instructions, cause conditions of faulty encoding, either because the gene's protein messenger is missing or incomplete. The disorders that result often become more severe over time as the malfunction continues to repeat itself. CYSTIC FIBROSIS, SICKLE CELL DISEASE, Duchenne's MUSCULAR DYSTROPHY, HUNTINGTON'S DISEASE, and MARFAN SYNDROME are single-gene disorders.

Multifactorial Disorders

Researchers suspect many health conditions arise as a result of an interplay between genetic and environmental factors. Geneticists call such conditions multifactorial disorders because it appears a certain combination of events must take place for disease to result; doctors may refer to them as conditions of GENETIC PREDISPOSITION. These are the conditions that tend to run in families; some family members develop them and others do not. Health conditions in which genetics, lifestyle, and other variables participate in the development of disease are numerous. Some of those that are common include CORONARY ARTERY DISEASE (CAD), HYPERTENSION (high BLOOD PRESSURE), CANCER, DIABETES, GALLBLADDER DISEASE, and NEPHROLITHIASIS (kidney stones), and numerous other conditions.

Mitochondrial Disorders

Mitochondria are self-replicating structures within a cell (called organelles) that carry out the metabolic functions of the cell. Mitochondria have their own DNA that directs their specific functions, and have multiple copies; MITOCHONDRIAL DNA (MTDNA) is different from the cell's nuclear DNA. MITOCHONDRIAL DISORDERS, which are the rarest of the genetic disorders, occur when the genes that encode mitochondrial activity contain mutations or when there are defects in the mtDNA. Mitochondrial disorders tend to vary widely among individuals, causing different symptoms because they affect different, and usually multiple, organs or structures. Doctors define the disorder as a complex of symptoms. Some forms of ENCEPHALOPATHY, MYOPATHY, and CARDIOMYOPATHY are mitochondrial disorders.

See also CONGENITAL ANOMALY; INHERITANCE PATTERNS; MOSAICISM.

genetic imprinting The inactivation of certain genes, determined by whether the GENE is maternal (comes from the mother) or paternal (comes from the father). Genetic imprinting, also called genomic imprinting, appears to be another method of controlling genes by requiring one copy of each of certain chromosomes from each parent.

INHERITANCE PATTERNS, which establish gene expression through dominance, regulate most gene expression and normally present paired chromosomes that determine which traits are expressed in the PHENOTYPE. However, it is possible for mutations to occur that result in both sets of a particular chromosome coming from the same parent (uniparental disomy). Though such mutations likely occur with no noticeable effect and thus remain undetected, they can allow rare recessive abnormalities to be expressed.

Though rare, the CHROMOSOMAL DISORDERS Prader-Willi syndrome and Angelman syndrome represent the most common pathology of genetic imprinting. These syndromes reflect uniparental disomy of CHROMOSOME 15, one of the chromosomes known to incorporate genetic imprinting. Chromosome 15 regulates numerous neurologic and musculoskeletal structures and functions that affect intelligence, cognition (the ability to think, reason, and remember), behavior, emotion, physical appearance, MUSCLE tone, movement, and METABOLISM as well as reproductive health and capability.

Normal development requires one copy of chromosome 15 from each parent. When both copies of chromosome 15 are maternal (called paternal deletion), genetic imprinting produces a constellation of symptoms known as Prader-Willi syndrome. When both copies of chromosome 15 are paternal (called maternal deletion), genetic imprinting produces a constellation of symptoms known as Angelman syndrome. Each syndrome presents differing manifestations of neurologic dysfunction, musculoskeletal and other physical anomalies, and intellectual impairment.

Researchers believe genetic imprinting is a mechanism intended to prevent damaging mutations from propagating (extending themselves). Genetic imprinting appears to affect only certain chromosomes and, when it causes a disease state, results in related though differing symptoms, depending on the deletion.

See also CELL STRUCTURE AND FUNCTION.

genetic predisposition The tendency to develop a health condition as a consequence of the interaction between genetics and lifestyle factors. Doctors believe genetic influences underlie many if not all health conditions that develop over time, such as HYPERTENSION (high BLOOD PRESSURE), ATHEROSCLEROSIS, OSTEOARTHRITIS, RENAL FAILURE, LIVER dis-

ease, and type 2 DIABETES. An individual's GENOTYPE establishes genetic vulnerability through mechanisms researchers do not fully understand.

These genetic elements influence the effects of environmental factors such as cigarette smoking, physical activity and inactivity, exposure to chemical toxins, ALCOHOL consumption, and nutrition (lack of certain NUTRIENTS or excesses of other nutrients) in the development of disease processes. Once the disease becomes established, its genetic underpinnings may allow more rapid progression of damage or severity of symptoms.

Unlike GENETIC DISORDERS that encode for specific disturbances of structures and functions that inevitably produce a disease state (such as DOWN SYNDROME), genetic predisposition for a condition does not make that condition certain. Many doctors and researchers believe knowing of genetic predispositions gives an individual the opportunity to engage in lifestyle modifications to prevent health problems from developing.

See also LIFESTYLE AND HEALTH.

genetic screening Procedures that indicate whether an individual has the potential to have a genetic disorder. Among the most commonly performed genetic screening procedures in the United States are prenatal ULTRASOUND and maternal BLOOD levels of multiple biomarkers, such as ALPHA FETOPROTEIN (AFP), during PREGNANCY. These procedures may present suspicious findings though are not precise enough to allow diagnosis. Other genetic screening procedures are those that test for conditions that occur in the general population and have significant consequences when undetected and untreated. For example, hospitals in the United States conduct routine newborn testing for PHENYLKETONURIA (PKU), an inherited metabolic disorder that results in severe intellectual impairment without treatment at the time of birth.

The findings of genetic screening, positive or negative, can have a margin of error for false-negative as well as false-positive results. However, doctors use genetic screening when factors of increased risk for GENETIC DISORDERS, such as maternal age in pregnancy or family history, exist. The doctor may conduct further GENETIC TESTING and diagnostic testing when the overall health picture points to an increased risk for genetic disorders, even when the findings of genetic screening procedures appear normal. Genetic screening procedures are minimally invasive and typically present no risk to the mother or the fetus in prenatal screening or to the individual in screening conducted following birth or in adults.

See also AMNIOCENTESIS; AUTOSOMAL TRISOMY; CHORIONIC VILLI SAMPLING (CVS); CHROMOSOMAL DISORDERS; ETHICS IN GENETICS AND MOLECULAR MEDICINE; FAMILY PLANNING; FOLIC ACID SUPPLEMENTATION; GENETIC TESTING; NEURAL TUBE DEFECTS.

genetic testing Methods and procedures to determine the presence of a genetic disorder. The KARYOTYPE, which uses microphotographs to examine and depict an individual's chromosomes, is one of the more common methods of genetic testing. Other methods include cytogenic analysis, AMNIOCENTESIS, and CHORIONIC VILLI SAMPLING (CVS). Some genetic testing methods are highly sophisticated and require specialized equipment and knowledge available only in research centers. Other methods, such as CVS, have become fairly commonplace.

Diagnostic genetic testing can identify the cause of symptoms resulting from GENE mutations and CHROMOSOMAL DISORDERS. This knowledge can be helpful when there are treatments and treatment choices for the resulting conditions, and in FAMILY PLANNING decisions. The matter of genetic testing to screen for the presence of GENETIC DISORDERS, particularly in people who do not have symptoms or apparent increased risk for conditions of genetic origin, remains an issue of intense ethical debate. Some such practices, such as testing for PHENYLKETONURIA (PKU) in newborns, have become standard in the United States. Others, such as those for the so-called CANCER genes (BRCA-1, BRCA-2, CA-125, and others), often raise more questions than answers because the consequence of having such genes remains uncertain.

Even when the outcome is certain, the knowledge of the genetic disorder may have little therapeutic value yet create distress for the individual. This is currently a significant issue with genetic testing for HUNTINGTON'S DISEASE, for example, a fatal neurodegenerative disorder for which there is no treatment or cure. People who carry the gene MUTATION for Huntington's disease are certain

to develop the disease in midlife. GENETIC COUNSELING is almost always a valuable and necessary component of genetic testing.

See also ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; GENETIC PREDISPOSITION; LIFESTYLE AND HEALTH.

genome The total genetic material, including coding and noncoding sequences, a cell contains in its chromosomes. Each organism has a unique genome. Scientists define the size of a genome by the number of its base pairs. The human genome contains 3.2 billion base pairs, which make up that comprise about 23,000 genes.

See also CELL STRUCTURE AND FUNCTION; CHROMOSOME; GENE; GENOTYPE; HUMAN GENOME PROJECT; PHENOTYPE.

genotype The contents of an individual's GENETIC CODE. The genotype directs the structures and functions of the human body. A person's genotype is to the human body what an architect's blueprint is to a house: It provides the directions for the construction and operation of the human organism.

See also GENOME; KARYOTYPE; PHENOTYPE.

G6PD deficiency An inherited genetic disorder in which the body lacks the enzyme glucose-6-phosphate dehydrogenase (G6PD). Erythrocytes (red BLOOD cells) normally produce G6PD, which aids in metabolizing carbohydrates and also helps to protect erythrocytes from oxidation (damage resulting from metabolic waste). The absence of G6PD causes health problems when the body experiences unusual stress, such as illness, or with certain medications such as aspirin and sulfa antibiotics. These circumstances cause oxidants to accumulate in the blood. Without G6PD to neutralize these oxidants, they destroy erythrocytes, resulting in hemolytic ANEMIA.

The symptoms of hemolytic anemia resulting from G6PD deficiency include

- dark URINE
- pale SKIN
- weakness
- JAUNDICE (yellowish discoloration of the skin and sclera of the eyes)
- HEPATOMEGALY (enlarged LIVER) and SPLENOMEGALY (enlarged SPLEEN)
- tachycardia (rapid HEART RATE)
- FEVER

Symptoms and family history may cause the doctor to suspect G6PD deficiency. Blood tests will reveal the hemolytic anemia. Treatment generally consists of avoiding circumstances and substances that trigger oxidative stress. Many people are able to avoid symptoms entirely through such an approach. Because G6PD is an inherited condition, there are no methods for prevention. The inheritance pattern for G6PD is X-linked recessive; G6PD affects twice as many males as females and is more prominent in people of African American heritage and Mediterranean heritage.

See also ERYTHROCYTE; GENETIC DISORDERS; INHERITANCE PATTERNS; PHENYLKETONURIA (PKU); PORPHYRIA.

H–K

Human Genome Project A collaborative undertaking among researchers around the world, organized under the joint auspices of the U.S. Department of Energy and the National Institutes of Health, to identify and map the human GENOME (genetic material that defines the human being). Altogether, more than 20 research centers in the United States, United Kingdom, China, France, Germany, and Japan participated in the DNA sequencing. The Human Genome Project began in 1990 and concluded with the full mapping of the human genome in April 2003, 50 years after Watson and Crick unveiled their double-helix model of DNA. Researchers expect data analysis and new findings to continue for the indefinite future. The Human Genome Project's Web site, (www.ornl.gov), regularly posts updates.

HUMAN GENOME PROJECT FINDINGS: HIGHLIGHTS

- The human GENOME consists of 3,164,700,000 NUCLEOTIDE bases.
- The largest GENE (dystrophin) contains 2.4 million nucleotide bases.
- 99.9 percent of the nucleotide bases are identical in all people.
- The human genome contains about 30,000 genes.
- CHROMOSOME 1 contains 2,968 genes and chromosome Y contains 231 genes, the most and the fewest, respectively.

Source: The Science behind the Human Genome Project, *www.ornl.gov/hgmis; updated October 27, 2004.*

See also CELL STRUCTURE AND FUNCTION; CLONING; ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; GENOTYPE; PHENOTYPE; RECOMBINANT DNA.

inheritance patterns The ways in which genotypes pass among individuals and generations. Many inherited traits are either autosomal or X-linked and either dominant or recessive. Such inheritance patterns reflect statistical calculations assessing the mathematical likelihood of certain traits or mutations passing from one generation to the next. Inheritance patterns consider the genotypes of each parent. Inheritance patterns vary according to whether the chromosomes responsible are autosomesal or sex-linked chromosomes. Geneticists often refer to these patterns as Mendelian, in reference to the foundational work of botanist Gregor Mendel (1822–1884), who was the first to delineate inheritance patterns.

Recent research, notably through the HUMAN GENOME PROJECT, has shown that much of human inheritance may not be quite so simple as the Mendelian model. Multiple genes and chromosomes share responsibility for traits ranging from EYE color to the development of diseases, such as DIABETES AND CARDIOVASCULAR DISEASE, that also have environmental (lifestyle) components. This circumstance of multiple factors makes it far more difficult to statistically represent a delineated pattern of inheritance. Multifactorial inheritance is not clearly dominant or recessive, though is commonly autosomal (derives from autosomes rather than sex chromosomes).

The least common pattern of inheritance is mitochondrial, which comes only from the mother and involves traits and mutations affecting mitochondrial, not nuclear, DNA. This pattern is exclusively maternal because only the ovum (female GAMETE or egg) contains mitochondria. Mitochondria affect functions rather than structures of the body, and thus, mitochondrial mutations cause numerous, nonspecific multisystem disturbances. Because mitochondria are the energy generators of the cells, mitochondrial mutations affect functions that require energy

INHERITANCE PATTERNS: AUTOSOMAL TRAITS AND MUTATIONS

Autosomal Recessive		Autosomal Dominant	
Both parents carriers	One parent carrier, one parent noncarrier	Both parents affected	One parent affected, one parent unaffected
Each child: 25% condition 25% noncarrier 50% carrier	Each child: 50% noncarrier 50% carrier	Each child: 25% unaffected 25% more severely affected than parents 50% affected	Each child: 50% unaffected 50% affected

Percentages refer to the probability of occurrence.

INHERITANCE PATTERNS: X-LINKED TRAITS AND MUTATIONS

X-Linked Recessive		X-Linked Dominant	
Mother CARRIER, father noncarrier	Mother noncarrier, father affected	Mother affected, father noncarrier	Mother noncarrier, father affected
Each daughter: 25% noncarrier 25% carrier	Each daughter: 100% carrier	Each daughter or son: 50% affected 50% nonaffected	Each daughter: 100% affected
Each son: 25% noncarrier 25% affected	Each son: 100% noncarrier		Each son: 100% nonaffected

Percentages refer to the probability of occurrence.

rather than affect structures of the body. Though mitochondrial mutations may be single-GENE, they often have widespread effects across types of cells in which energy needs are high, such as NERVE cells and MUSCLE cells.

See also AUTOSOME; CHROMOSOME; FAMILY MEDICAL PEDIGREE; GENOTYPE; MITOCHONDRIAL DISORDERS; MITOCHONDRIAL DNA (MTDNA); MUTATION; SEX CHROMOSOME.

karyotype A pictorial presentation of an individual's chromosomes, taken from microphotographs (photographs taken through a microscope) and arranged in a numeric sequence that aligns the chromosomes from largest to smallest. This standardized presentation allows the geneticist to analyze an individual's chromosomal profile. A geneticist can structure a karyotype from any SOMATIC CELL (nonsex cell) in the body. The most common application of karyotyping is GENETIC SCREENING of a fetus. A geneticist constructs a karyotype to evaluate whether an individual has a GENETIC DISORDER. A karyotype requires DNA from a representative cell in the body, from which the geneticist extracts and prepares the DNA for examination under the microscope.

See also CHROMOSOME; GENETIC COUNSELING; GENETIC DISORDERS; GENETIC TESTING.

M–N

mitochondrial disorders Inherited mutations in mitochondrial genes that result in functional disturbances in various body systems. Mitochondria are structures within the cell that generate the energy, in the form of adenosine triphosphate (ATP), the cell requires to function. A cell may contain dozens of mitochondria. Each mitochondrion contains the specific genetic material (MITOCHONDRIAL DNA [MTDNA]) to encode the enzymes (specialized proteins) that regulate the biochemical reactions within the mitochondrion that generate ATP. The only function of mtDNA is to regulate these processes of energy production.

Each mitochondrion contains multiple copies of its DNA. Mutations typically affect some but not all DNA copies, so mitochondrial function continues though may be impaired whenever the mutated mitochondrial GENE sends incorrect code. Only the ovum contains mitochondria that pass on to the ZYGOTE at CONCEPTION. SPERM cells contain few mitochondria, and these are in the sperm cell's tail, which breaks away as soon as the sperm penetrates the ovum. As the zygote continues to divide, it may perpetuate errors in mtDNA that are widespread or pervasive.

Mitochondrial disorders include myositis, some types of CARDIOMYOPATHY, some types of MYOPATHY, and carnitine deficiency syndrome. Often, symptoms are multisystem and inconsistent with the conventional presentations of the health conditions they suggest. MUSCLE and NERVE cells have particularly high energy needs, so mitochondrial disorders often manifest symptoms such as weakness and poor muscle tone (hypotonia).

Because mitochondrial disorders are rare and their symptoms are confusing, the diagnostic path may lead to numerous dead ends. Though this process rules out other diagnoses, it is a frustrating experience for those patients looking for answers for their symptoms. There are no definitive diagnostic tests for mitochondrial disorders, though muscle biopsy often can provide strong evidence supporting diagnosis once doctors rule out other conditions and disorders. Treatment targets managing symptoms and preventing common complications such as DEHYDRATION. Some doctors advocate COENZYME Q10 supplementation for people who have mitochondrial disorders, which appears to improve the efficiency of cellular METABOLISM as well as protect cells from oxidative damage. People who have mitochondrial disorders should include GENETIC COUNSELING in their FAMILY PLANNING efforts.

See also CELL STRUCTURE AND FUNCTION; CHROMOSOME DISORDERS; GENETIC DISORDERS; MUTATION; REPLICATION ERROR.

mosaicism A chromosomal disorder in which some cells are normal and some cells contain the chromosomal abnormalities of the disorder, in contrast to a complete distribution of the abnormal chromosomes throughout all cells. The distribution of abnormal cells in mosaicism is usually random and unpredictable. Mosaicism most commonly occurs in AUTOSOMAL TRISOMY, in which there is an additional copy of one CHROMOSOME that appears in some cells and not in others. The result generally is a milder presentation of symptoms when only some cells express the abnormality (mosaic disorder) than occurs when all cells express the abnormality (complete disorder). People who have a mosaic expression of the autosomal trisomy disorder DOWN SYNDROME, for example, typically have milder symptoms than people who have a complete expression. Mosaicism may also affect genetic expressions other than health disorders.

See also CELL STRUCTURE AND FUNCTION; CHROMOSOMAL DISORDERS; EDWARDS SYNDROME; INHERITANCE PATTERNS; MUTATION; PATAU'S SYNDROME; REPLICATION ERROR.

mutation Permanent alterations in the ALLELE pairings, or genes, on the chromosomes that pass on to new cells and ultimately to offspring. Mutations are the process through which genetic change takes place. Some mutations are beneficial, some are neutral, and some are harmful. Mutations occur as changes in the GENE's NUCLEOTIDE sequences. These changes may take the form of

- point mutations, also called base mutations, which are analogous to changing one letter in a word and occur when one nucleotide substitutes for another
- deletion mutations, which are analogous to removing a word from a sentence and occur when the gene drops a nucleotide sequence
- insertion mutations, which are analogous to adding a word to a sentence and occur when the gene adds a nucleotide sequence
- increased repeat mutations, which occur when a normally repeated nucleotide repeats extra times

A germline mutation affects a GAMETE (ovum or spermatozoon) or ZYGOTE and is present from CONCEPTION, passing to the child. WILMS'S TUMOR and HEMOPHILIA are examples of germline mutations that cause disease. A monogenic MUTATION affects a single gene. Duchenne's MUSCULAR DYSTROPHY and SICKLE CELL DISEASE are among the conditions that occur as a result of monogenic mutations. Polygenic mutations involve multiple alleles of numerous genes, often across chromosomes. Polygenic mutations often do not clearly result in GENETIC DISORDERS though establish GENETIC PREDISPOSITION. Conditions such as CARDIOVASCULAR DISEASE (CVD), DIABETES, and some types of cancer occur as a result of polygenic mutations in combination with lifestyle (environmental) factors.

See also AUTOSOMAL TRISOMY; CHROMOSOMAL DISORDERS; LIFESTYLE AND HEALTH.

nucleotide A structural component of DNA and RNA. A DNA nucleotide contains deoxyribose and a nitrogen base of adenine, guanine, thymine, or cytosine, which form pairs called base pairs. An RNA nucleotide contains ribose and a nitrogen base of paired adenine, guanine, uracil, or cytosine. Each DNA or RNA molecule contains thousands of nucleotides. The order in which the nucleotides appear is the base sequence and conveys the GENETIC CODE for the proteins the DNA or RNA molecule encodes. Base sequences, arranged in triplets (trinucleotides), make up GENES.

See also CELL STRUCTURE AND FUNCTION; CHROMOSOME; GENOME.

P–R

Patau's syndrome An AUTOSOMAL TRISOMY disorder that results from a REPLICATION ERROR during cell division in which a GAMETE (sex cell) ends up with two copies of CHROMOSOME 13 instead of the normal single copy (as haploid cells, gametes contain one-half the complement of chromosomes). At CONCEPTION the ZYGOTE thus ends up with three instead of the normal two copies of chromosome 13, which ultimately produces multiple and life-threatening congenital anomalies. When Patau's syndrome occurs as a complete trisomy disorder (all cells carry the extra chromosome), the anomalies are so severe that the disorder often is lethal well before birth. Occasionally Patau's syndrome occurs as a mosaic disorder (some but not all cells contain the extra chromosome 13), which typically produces milder though nonetheless significant symptoms. Patau's syndrome occurs in about 1 in 10,000 live births in the United States.

CONGENITAL ANOMALIES CHARACTERISTIC OF PATAU'S SYNDROME

atrial septal defect (ASD)	CLEFT PALATE/CLEFT PALATE AND LIP
malformed KIDNEYS	malformed KIDNEYS
malformed or absent eyes	microcephaly (small head and BRAIN)
malformed or absent NOSE	polycystic kidneys
multiple hernia	POLYDACTYLY
patent ductus arteriosus (PDA)	vextrocardia (HEART on right side of chest)
ventricular septal defect (VSD)	

Children born with Patau's syndrome have severe and complex physical deformities involving multiple organ systems that require extensive medical care from the time of birth. Most also have severe developmental delays and intellectual impairment arising from malformations affecting the BRAIN and NERVOUS SYSTEM. KARYOTYPE confirms the diagnosis. It is rare for a child who has Patau's syndrome to survive beyond early childhood; there are no documented survivals to adulthood. Ongoing medical care to accommodate physical anomalies and developmental support to achieve optimal learning potential provide the child who survives the best possible QUALITY OF LIFE.

See also AUTOSOME; CHROMOSOME DISORDERS; CONGENITAL ANOMALY; CONGENITAL HEART DISEASE; DOWN SYNDROME; EDWARDS SYNDROME; ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; GENETIC SCREENING; INHERITANCE PATTERNS; MOSAICISM; POLYCYSTIC KIDNEY DISEASE.

phenotype The outward presentation, or features, of an individual's GENOTYPE (genetic composition). The phenotype is the construction and operation that results from implementation of the genotype, much as a house is the outcome of a building contractor's implementation of an architect's blueprints. A phenotype consists of such obvious characteristics as EYE color and HAIR patterns as well as less apparent traits such as BLOOD TYPE and proclivity for health or certain diseases. The genotype for lipid METABOLISM, for example, may support effective use of lipids within the body (supporting health) or the tendency for high levels of lipids to accumulate in the BLOOD (increasing the risk for CARDIOVASCULAR DISEASE [CVD]).

See also ALLELE; ALOPECIA; CELL STRUCTURE AND FUNCTION; FAMILY MEDICAL PEDIGREE; VARIATION.

phenylketonuria (PKU) An inherited genetic disorder in which the enzyme phenylalanine hydroxylase is missing or severely deficient, preventing the METABOLISM of the essential amino acid (one the body must acquire from dietary sources)

phenylalanine. Phenylalanine is common in all foods that contain protein (such as meats, dairy products, fish, and legumes) and in artificial sweeteners such as aspartame. Avoiding foods that contain phenylalanine, which means following a strict low-protein diet, prevents phenylalanine accumulations and the resultant damage that affects primarily the NERVOUS SYSTEM. The most significant consequence of undiagnosed PKU is irreversible, and usually severe, intellectual impairment.

Symptoms and Diagnostic Path

Early symptoms of PKU appear soon after birth and include restlessness, irritability, stunted growth, and a characteristic musty smell to the breath. The appearance of symptoms means neurologic damage is already occurring, however. Newborn screening to identify PKU before symptoms appear is essential to prevent intellectual impairment. Hospitals in the United States routinely screen newborns, typically within two days of birth, to detect elevated levels of phenylalanine in the blood. Further testing can confirm the diagnosis, and immediate dietary restrictions can prevent the disorder from causing permanent damage.

Treatment Options and Outlook

Treatment is stringent restriction of dietary phenylalanine, which includes BREAST milk. Infants require special phenylalanine-free formulas. Dietary restrictions are lifelong. Many food products contain labeling information that states their phenylalanine content, and a number of food manufacturers produce low-phenylalanine versions of popular foods such as cereals as well as phenylalanine-free protein substitutes. Fruits, vegetables, breads, and pastas contain very low amounts of phenylalanine. In the United States foods that contain aspartame must state on the label that they contain phenylalanine.

Women who have PKU can safely carry a PREGNANCY to term though must be especially diligent to maintain a low phenylalanine diet because excessive phenylalanine in the mother's BLOOD circulation also affects the developing FETUS and can cause permanent neurologic and other damage before birth. Because the inheritance pattern for PKU is autosomal recessive, women who have PKU will pass the disorder to their children only if the father carries the mutated gene or also has PKU.

Risk Factors and Preventive Measures

PKU is an autosomal recessive, single-GENE mutation. Both parents must carry the PKU mutation for a child to have the disorder. However, PKU carriers often do not know they have the mutated gene because they do not show any indications of the disorder. People who know they are PKU carriers or who have PKU should consider GENETIC COUNSELING as an element of their FAMILY PLANNING.

See also CARRIER; GENETIC DISORDERS; INHERITANCE PATTERNS; NUTRITIONAL NEEDS; PORPHYRIA.

porphyria The collective term for a group of eight inherited GENETIC DISORDERS of METABOLISM in which deficiencies of certain enzymes block the production of heme and allow the accumulation of porphyrins. Heme is an iron-containing pigment normally present in nearly all tissues in the body, notably as a component of HEMOGLOBIN in the BLOOD and of electron transport proteins called cytochromes. The LIVER produces cytochromes, which are essential for metabolizing numerous drugs, hormones, NUTRIENTS, and other substances. Heme synthesis occurs in a sequence of eight steps, each occurring through the actions of a particular enzyme. Each of the eight forms of porphyria represents the absence of one of these enzymes.

Symptoms and Diagnostic Path

Symptoms vary with the type of porphyria and may be neurologic (affect the NERVOUS SYSTEM), dermatologic (affect the SKIN), hepatic (involve the liver), or erythropoietic (involve the BONE MARROW and blood). Typically symptoms are episodic, occurring as attacks that last for days to weeks and sometimes longer. Symptoms vary widely in appearance, severity, and duration and may include

- eruptive skin rashes (bullae)
- PHOTOSENSITIVITY
- severe ABDOMINAL PAIN
- NAUSEA, VOMITING, and DIARRHEA
- MUSCLE weakness and possibly PARALYSIS
- agitation and hallucinations

THE PORPHYRIAS

Porphyria	Deficient Enzyme	Inheritance Pattern
acute intermittent porphyria (AIP)	porphobilinogen deaminase (PBG-D)	autosomal dominant
ALAD-deficiency porphyria (ADP)	aminolevulinic acid dehydratase (ALAD)	autosomal recessive
congenital erythropoietic porphyria (CEP)	uroporphyrinogen III cosynthase	autosomal recessive
erythropoietic protoporphyria (EPP)	ferrochelatase	autosomal dominant
hepatoerythropoietic porphyria (HEP)	uroporphyrinogen decarboxylase	autosomal recessive
hereditary coproporphyria (HCP)	coproporphyrinogen oxidase	autosomal dominant
porphyria cutanea tarda (PCT)	uroporphyrinogen decarboxylase	autosomal dominant
variegate porphyria (VP)	protoporphyrinogen oxidase	autosomal dominant

- tachycardia (rapid HEART RATE)
- URINARY RETENTION and URINARY INCONTINENCE

The diagnostic path includes blood and urine tests to measure the presence of key porphyric enzymes. In people who know they have porphyria, exposure to identified precipitating factors—which include numerous drugs, hormones, and nutrients—will bring on an attack. HYPERTENSION (high BLOOD PRESSURE) can develop during an attack and persist after symptoms subside.

Treatment Options and Outlook

Severe symptoms, particularly neurologic, require hospitalization and aggressive treatment that may include intravenous heme administration (the only form in which heme is available). Medications safe to take to relieve and control symptoms include narcotic pain relievers and phenothiazines to relieve nausea and vomiting or neuropsychiatric symptoms. It is crucial to stop any substances that may have precipitated the attack. Most symptoms subside within two to three weeks, and most people fully recover within six weeks. Some people experience extended muscle weakness. Attacks may occur without provocation. Many people who have porphyria seldom experience attacks, however.

Risk Factors and Preventive Measures

The porphyrias are inherited genetic disorders. The risk of porphyria depends on the inheritance pattern. There are no measures to prevent porphyria. People who have porphyria, or who have family members who have porphyria, might consider GENETIC TESTING and GENETIC COUNSELING. It is possible to be a CARRIER for the autosomal recessive forms of porphyria.

See also BULLA; CYTOCHROME P450 (CYP450) ENZYMES; GENE; HALLUCINATION; HORMONE; MUTATION; RASH.

progeria A very rare genetic disorder, commonly called severe premature aging, that arises from a MUTATION in a single GENE on CHROMOSOME 1 called lamin A (LMNA). The gene encodes a protein, also called lamin A, that is important for proper functioning of the membrane of the cell nucleus. In progeria this protein is abnormal, resulting in rapid deterioration of the nuclear membrane and destruction of the cell. The diagnostic path is primarily clinical, based on symptoms. Most children who have progeria die of cardiovascular problems such as HEART ATTACK or STROKE by the age of 12 or 13 years. As a consequence of research into the causes of progeria, scientists have discovered other mutations of the same gene that cause uncommon

forms of MUSCULAR DYSTROPHY. At the present time there is no treatment, cure, or prevention for progeria.

See also CELL STRUCTURE AND FUNCTION; GENETIC DISORDERS.

recombinant DNA A biotechnology technique that replaces DNA to alter a cell's function. There are several methods for performing recombination, though all ultimately involve extracting the native DNA from a carrier (called a vector) and replacing it with the desired DNA. Modified BACTERIA and viruses are common vectors—bacteria because they replicate rapidly, and viruses because they can deliver modified DNA into the nucleus of cells within the body (GENE THERAPY).

One of the most significant uses of recombinant DNA technology is the production of substances such as human INSULIN supplementation to treat DIABETES, which recombinant technology can synthesize in vast quantities in the laboratory to meet strict quality and consistency standards. Because such recombinant products are biochemically indistinguishable from their endogenous (naturally produced in the body) counterparts, they are an exact replacement, and the body accepts them as though they were endogenous. Recombinant DNA technology produces other hormones, too, such as HUMAN GROWTH HORMONE (HGH) SUPPLEMENT.

See also CELL STRUCTURE AND FUNCTION; CLONING; HORMONE; VIRUS.

replication error A mistake that occurs when DNA sequences duplicate before cell division. Replication errors are accountable for CHROMOSOMAL DISORDERS such as AUTOSOMAL TRISOMY, in which a GAMETE (also called a sex cell or germ cell) receives two copies of a CHROMOSOME instead of the normal single copy. Gametes, which are haploid cells, each carry one-half the complement of chromosomes so when they unite to form the ZYGOTE that will become a new human being, the zygote contains the full complement of genetic material. With a replication error such as an autosomal trisomy, the zygote receives an extra chromosome—two copies from one gamete and one copy from the other gamete. The result is a chromosomal disorder such as DOWN SYNDROME. Replication errors also may have harmless consequences when they occur in DNA sequences that do not encode structural or regulatory sequences of gene activity.

See also MUTATION; VARIATION.

RNA The abbreviation for ribonucleic acid. RNA is a single-strand molecule consisting of ribose; a sugar; and nucleotides made up of the nitrogen bases adenine, uracil, guanine, and cytosine. RNA exists in a number of forms, all of which serve as biochemical messengers that carry the instructions of DNA to the ribosomes, structures in the cell's cytoplasm. Ribosomes synthesize (manufacture) the proteins the genes encode. RNA also may function as the carrier of GENETIC CODE within the mitochondria.

For further discussion of RNA within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CELL STRUCTURE AND FUNCTION; GENE; NUCLEOTIDE.

S

senescence The gradual and progressive slowing of cellular activity, including cell division, that occurs with aging. Cells lose the ability to divide over time, a phenomenon researchers call Hayflick's limit. The limit relates to the number of times the cell divides. During cell division, fibers of DNA called telomeres attach to the chromatids, facilitating their separation from each other to enter the new daughter cells. The process destroys the segment of the TELOMERE attached to the CHROMATID, causing the telomere to shorten with each cell division. When the cell runs out of telomeres it can no longer divide and it dies.

The exceptions are cancer cells, which seem to be nonsenescent. Cancer cells produce increased levels of an enzyme called telomerase, which acts to restore the length of the telomeres and gives cancer cells the ability to endlessly divide. Normal cells also produce telomerase but not in quantities sufficient to regenerate telomeres. Researchers do not know what causes cancer cells to increase the amount of telomerase they produce. As well, other factors are at play in the processes of senescence, which researchers continue to study.

See also APOPTOSIS; CELL STRUCTURE AND FUNCTION; PROGERIA.

sex chromosome The structure of GENETIC CODE that determines gender (male or female). The male sex CHROMOSOME has the appearance of the letter *Y* and the female sex chromosome has the appearance of the letter *X*. A combination of XY results in male and a combination of XX results in female. The Y chromosome contains fewer than 100 genes, while the X chromosome carries several hundred genes. A number of GENETIC DISORDERS are X-linked—that is, they result from mutations that occur among genes the X chromosome carries. HEMOPHILIA and some forms of MUSCULAR DYSTROPHY (notably Duchenne's and Becker's) are X-linked genetic disorders.

See also AUTOSOME; GAMETE; GENE; MUTATION; SOMATIC CELL.

somatic cell A cell that is not a GAMETE (sex cell). More than 99 percent of the body's trillions of cells are somatic cells. Somatic cells are diploid; their nuclei contain the full complement of paired chromosomes and genetic material necessary to encode an organism. When somatic cells divide, their chromosomes replicate so the new daughter cells receive the full complement of paired chromosomes as well.

For further discussion of somatic cells within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CELL STRUCTURE AND FUNCTION; CHROMOSOME; CONCEPTION; REPLICATION ERROR; ZYGOTE.

stem cell An undifferentiated, primal cell that has the capability to endlessly divide and develop into numerous types of cells. Totipotent stem cells exist primarily in the early EMBRYO (blastocyst) and can differentiate into (become) virtually any type of cell in the body. As the body becomes more complex and develops beyond the blastocyst stage, stem cells become specialized to produce certain kinds of cells, which they retain the ability to do endlessly. These stem cells, though found in tissues of all kinds throughout the body, are most highly concentrated in the BONE MARROW (BLOOD STEM CELLS). UMBILICAL CORD BLOOD is another source of highly concentrated blood stem cells. Blood stem cells can differentiate into any type of blood cell.

Researchers have had some success with stimulating blood stem cells, in the laboratory, to function as though they were other types of cells such as NERVE cells or MUSCLE cells, and are hopeful that stem cells will someday become a source of cultivated replacement tissues and organs. Multipotent stem cells that occur in other tissues are difficult to identify and extract from their source tissues though may also hold similar potential.

For further discussion of stem cells within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; GAMETE; HEMATOPOIESIS; STEM CELL THERAPY.

stem cell therapy Implantation of STEM CELLS to become specialized cells for tissue and organ repair or replacement. Though most STEM CELL therapy applications remain experimental, BONE MARROW TRANSPLANTATION (also called BLOOD stem cell transplantation) has become a standard of treatment for many cancers affecting the blood and the lymphatic system (leukemias and lymphomas) as well as certain other cancers. Researchers have also been successful in cultivating stem cells into SKIN for skin grafting, to treat severe BURNS, and into pancreatic islet cells that produce INSULIN, to treat severe type 1 DIABETES. Though these applications of stem cell therapy remain experimental, they raise the potential for stem cell therapy to become viable in treating numerous health conditions.

Two significant concerns with stem cell therapy are the potential for cancer to develop and the rejection of the cultivated cells or tissue. A prime value of the stem cell is its unlimited ability to divide. However, a function called APOPTOSIS limits most division of the cells in the body. It appears that cells can divide only a certain number of times, then begin to shut down. The exceptions are stem cells and cancer cells, and researchers are not certain what will keep stem cells from becoming cancer cells. Apoptosis remains a focus of much research. And as is the case with organs donated for transplantation, the body can reject stem cell transplantations. When this occurs the body's IMMUNE SYSTEM attacks the transplanted stem cells, killing them.

See also BLOOD STEM CELLS; CELL STRUCTURE AND FUNCTION; GENE THERAPY; ISLETS OF LANGERHANS; LEUKEMIA; MOLECULARLY TARGETED THERAPY.

T–Z

Tay-Sachs disease An inherited genetic disorder that causes a progressive, fatal form of gangliosidosis (the accumulation of gangliosides within NERVE cells). Tay-Sachs disease involves mutations of a pair of genes on CHROMOSOME 15 that encode for the enzyme hexosaminidase-A (hex-A). The mutation blocks production of hex-A. The body requires hex-A to metabolize GM2 ganglioside, a fatty acid that nerve cells need to metabolize and produce energy. Without adequate hex-A this METABOLISM cannot take place, and the GM2 ganglioside that enters the cell accumulates. GM2 ganglioside concentrations are highest within the nerve cells in the BRAIN as these nerve cells have the highest energy needs among nerve cells. GM2 ganglioside accumulates in other nerve cells as well. The accumulation causes the nerve cell to swell and eventually rupture.

Though the accumulation of GM2 ganglioside begins before birth, symptoms do not become apparent until age four to six months. Around this age the damage to brain tissue reaches a critical level and begins to disrupt brain activity. The child appears to regress developmentally. Brain function continues to decline, affecting intellectual and thought processes as well as voluntary and involuntary functions throughout the body. Tay-Sachs disease is usually fatal before age five years. An uncommon variation, late-onset Tay-Sachs disease, allows slight amounts of hex-A, delaying the onset of symptoms until ADOLESCENCE or early adulthood. However, the progressive loss of neurological and cognitive function follows a similar timeline once symptoms start.

Symptoms and Diagnostic Path

The earliest indication of Tay-Sachs disease is a characteristic round, cherry-red spot on the macula at the back of the EYE, the point where the ocular nerve joins the RETINA. The spot represents the onset of gangliosidosis in the optic nerve. Other symptoms include

- flaccid MUSCLE tone (early)
- loss of voluntary muscle control and movement (late)
- irritability (early)
- intellectual impairment
- seizures (late)
- diminishing responsiveness and awareness (progressive)
- loss of vision (progressive)

The diagnostic path includes family history, ethnic heritage, BLOOD tests to measure the level of hex-A present in the circulation, and GENETIC TESTING such as cytogenetic analysis and DNA sequencing. The genetic tests provide the definitive diagnosis.

Treatment Options and Outlook

There is no treatment or cure for Tay-Sachs disease. Nearly all children who have Tay-Sachs disease die before the age of five years. Research exploring methods to replace hex-A so far have been unsuccessful. Currently the most effective efforts target prevention by identifying carriers, who do not themselves have Tay-Sachs disease and who may not know they carry the GENE MUTATION.

Risk Factors and Preventive Measures

Tay-Sachs disease is an autosomal recessive disorder, meaning both parents must have the mutated gene for them to have a child with the disease, a one in four chance with each CONCEPTION. People

at highest risk for Tay-Sachs disease are those of Ashkenazi Jewish heritage. A blood test became available in 1985 to detect carriers of Tay-Sachs disease, who do not themselves have the disease but who have lower than normal amounts of hex-A in their blood. GENETIC COUNSELING can help couples who are carriers make informed decisions about whether to have children. Assisted reproductive technologies (ARTs) such as in vitro fertilization allow genetic testing before implantation so the couple knows the conceived child does not carry the mutated genes.

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); ETHICAL ISSUES IN GENETICS AND MOLECULAR MEDICINE; GENETIC CARRIER; GENETIC DISORDERS; INHERITANCE PATTERNS.

telomere A structure of noncoding DNA (DNA that does not convey genetic instruction) at each end of a CHROMOSOME. Telomeres are essential for chromosome duplication during cell division. They function as handles to pull the chromatids (dividing chromosomes) apart as the mother cell divides into the two new daughter cells. The process of cell division permanently destroys a tiny fragment of the telomere, however. Eventually the telomere becomes too short to participate in chromosome duplication, and the cell stops dividing. Researchers believe the shortening of telomeres is key to APOPTOSIS, the apparently programmed death of cells. In cancer cells the telomeres regenerate after cell division, which researchers believe is one of the factors that allows cancer cells to grow uninhibited.

For further discussion of telomeres within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also CELL STRUCTURE AND FUNCTION; CENTROMERE; CHROMATID; SENESCENCE.

translocation A chromosomal disorder in which a fragment of a CHROMOSOME breaks from its original chromosome and attaches itself to a different chromosome. The fragment may exchange with another fragment, may add itself to another chromosome, or may become lost. Some translocations are random and others occur in predictable patterns. Translocations can be reciprocal, in which chromosome fragments trade places with one another. Such balanced translocations are common and usually do not produce symptoms because all the normal genetic material remains within the GENOME.

A Robertsonian translocation occurs when the long arms of two acrocentric chromosomes, in which the CENTROMERE (waistlike indentation) is so high on the chromosome that the upper arms appear nonexistent and the upper arms contain almost no genetic material. Robertsonian translocations occur only among the five acrocentric chromosomes, which are chromosomes 13, 14, 15, 21 and 22. Like reciprocal translocations, Robertsonian translocations generally do not produce harmful consequences because the genetic material remains unadulterated despite the translocation. Robertsonian translocations are fairly common.

One reciprocal translocation that tends to produce harmful health effects is the Philadelphia chromosome, in which a segment of chromosome 9 and a segment of chromosome 22 exchange places. Geneticists commonly find this translocation in people who have chronic myeloid LEUKEMIA (CML).

See also CELL STRUCTURE AND FUNCTION; CHROMOSOMAL DISORDERS; DNA.

trisomy 13 See PATAU'S SYNDROME.

trisomy 18 See EDWARDS SYNDROME.

trisomy 21 See DOWN SYNDROME.

variation The genetic differences among individuals. There are trillions of possible GENE combinations within the human GENOME. Except for identical twins, no two people share exactly the same GENOTYPE (genetic constitution). Though any two individuals may have 99.9 percent of the same DNA sequences and gene pairings, the 0.1 percent of pairings that differ accounts for the endless details that make each individual unique.

The same genotype can have multiple expressions (phenotypes) among individuals. The genotype for EYE color, for example, can express itself as blue eyes in one person and brown eyes in another. Such variability exists for every gene

pairing, with more or less obvious results. VARIATION also occurs through MUTATION, in which DNA sequences change during replication. Polymorphisms and mutations may have positive, neutral, or negative effects, which differ among individuals based on circumstance, lifestyle, and other factors.

See also ALLELE; CELL STRUCTURE AND FUNCTION; GENETIC PREDISPOSITION; INHERITANCE PATTERNS; PHENOTYPE.

zygote The fertilized ovum (egg) before it begins to divide. The spermatozoon (SPERM cell) and the ovum are each haploid cells (gametes); they contain half the complement of chromosomes necessary to create an organism. When two gametes join they form a single diploid cell that contains the full complement of chromosomes. The zygote then divides as a haploid cell, becoming a blastocyst and eventually forming an EMBRYO.

For further discussion of zygotes within the context of the structures and functions of genetics, please see the overview section "Genetics and Molecular Medicine."

See also ASSISTED REPRODUCTIVE TECHNOLOGY (ART); CELL STRUCTURE AND FUNCTION; CHROMOSOME; CONCEPTION; GAMETE; OVULATION.

DRUGS

The area of health care concerned with drugs and medicinal therapies is pharmacology. Health-care professionals who dispense prescription drugs are pharmacists, who may be registered pharmacists (RPh) or doctors of pharmacy (PharmD).

This section, "Drugs," presents an overview discussion of pharmacologic concepts and entries about drugs and their use for the maintenance of health and the treatment of infection, injury, and disease.

Pharmaceutical Traditions in Medical History

The earliest written medical documents reference often elaborate preparations of botanicals used as medicines to treat a broad spectrum of ailments, ranging from HEADACHE and itching to weak PULSE and infected wounds. Healers in the times of ancient Babylonia, Mesopotamia, Egypt, and China relied on extensive collections of herbs, roots, barks, and seeds from which they concocted tinctures, teas, poultices, and other remedies. Ancient pharmacopeias outlined the formulations and uses of hundreds of plant forms for medicinal purposes.

ALCOHOL, too, was a major weapon in the early physician's pharmaceutical arsenal, serving as a topical antibacterial as well as an ingested analgesic (PAIN reliever) and quasi-anesthetic. Opium poppies and coca leaves yielded the first NARCOTICS, opium and COCAINE. Coffee beans and tea leaves yielded CAFFEINE, a potent stimulant. Tobacco leaves, chewed or smoked, were the source of another powerful stimulant, NICOTINE. Coca leaves and tobacco leaves acquired such high value in some early cultures that they served as currency.

Today medicinal herbs and botanicals remain the mainstay of TRADITIONAL CHINESE MEDICINE (TCM) and form the foundation of the modern pharmaceutical industry. As many as 5,000 medicinal plants grow in various regions around the world, many in the rain forests of South America. About 25 percent of modern medicines trace their derivations directly or indirectly to plants. Laboratories now produce synthetic forms of many drugs once extracted from plants, such as the antiarrhythmia DRUG digoxin (digitalis from the foxglove plant), the pain reliever aspirin (salicin from the bark of the willow tree), and the antimalarial drug quinine (quinaquina from the bark of the chinchona tree). Other drugs, such as the anticancer drug paclitaxel (Taxol), which is an extract from the bark of the Pacific yew tree, still derive from their botanical sources.

Drug Controls and Regulations

The regulation of drugs—from effectiveness and safety to production and availability—that is the foundation of today's pharmaceutical industry is a modern phenomenon. Until the early 20th century narcotics such as opium and HEROIN were freely available in the United States. Patent medicines (an odd assortment of liniments, elixirs, tinctures, nostrums, bitters, extracts, and compounds) dominated the druggist's apothecary. From Lydia E. Pinkham's Vegetable Compound, which contained far more alcohol than vegetable, to Mrs. Winslow's Soothing Syrup, a sedating preparation of morphine, patent medicines claimed to treat just about any ailment . . . and many claimed to treat just about *every* ailment.

The Pure Food and Drugs Act of 1906 was the beginning of the end for patent medicines; requiring medicine labels to list the product's ingredients and spawning the federal oversight agency that was to become the US Food and Drug Administration (FDA). In 1938 the Food, Drugs, and Cosmetics Act extended the authority of the FDA to regulate the safety and therapeutic effectiveness (and labeling claims thereof) of drugs, requiring manufacturers to prove a drug's safety before being allowed to market the drug. The regulations arose from the sometimes deleterious adulteration of drug products, brought to the forefront of public outrage when the use of poisonous wood alcohol in a sulfa preparation caused the deaths of more than 100 people. Shortly thereafter the FDA established separate classifications for prescription drugs and OVER-THE-COUNTER (OTC) DRUGS, prescription drugs being those whose safe use required a physician's oversight and guidance and OTC drugs being those that individuals could safely use without the guidance of a doctor or pharmacist.

Drug advertising remained under the jurisdiction of the Federal Trade Commission (FTC) until the Drug Amendments of 1962, the first of several key amendments to the Food, Drugs, and Cosmetics Act. The 1962 Drug Amendments also gave the FDA the regulatory authority to require evidence of a drug's safety as well as effectiveness before granting approval for the drug. The Dietary Supplements and Nutritional Labeling Act of 1994 drew back some authority from the FDA, however, reclassifying herbal and botanical products as dietary supplements and removing from FDA regulatory oversight.

Challenges in Pharmaceutical Therapy

Drugs have transformed health care over the past half century, relegating to insignificance many infections and diseases that in previous generations meant lifelong disability or early death. Drugs treat INFECTION, DIABETES, CARDIOVASCULAR DISEASE (CVD), kidney disease, LIVER disease, gastrointestinal disease, neurologic disorders, and cancer. Doctors in the United States write more than 14 billion prescriptions a year for nearly 3,000 different drugs, and another 2,000 medications are available in over-the-counter (OTC) products that are available without a doctor's prescription. Indeed, there are few health conditions for which there are not pharmaceutical treatments. Nonetheless, significant challenges exist. Health experts worry that the expense of drugs puts them out of reach for many people who need them and that collectively people are developing habits in regard to drug therapies that ultimately put health at greater risk.

Drug costs and availability Pharmaceutical manufacturers spend millions of dollars every year to develop new drugs. Yet as many as 20 promising drug concepts may die in the laboratory for every one that makes it clinical testing. For the length of time a drug remains under patent after its approval, an average of 14 years, the drug's manufacturer has an exclusive piece of a multibillion-dollar market. Though few dispute a pharmaceutical company's right to expect a financial return on its investment, the high cost of drugs still under patent makes the drugs unaffordable for many people. Older people take the hardest hit, caught in an intersection between increasing health-care needs and a fixed income.

One major effort to reduce drug costs is generic drugs, which are identical to their trade name counterparts (innovator drugs) in terms of active ingredients, DOSE, form, and efficacy (action in the body). The Government Accountability Office (GAO), the official expenditure watchdog of the federal government, estimates that generic drugs save Americans more than $10 million a year.

The high cost of drugs in the United States has fueled interest in purchasing drugs from countries in which they are not as expensive, such as Canada and Mexico. Although US law prohibits bringing imported drugs into the country, many people order them from Internet and mail-order sources nonetheless to save hundreds to thousands of dollars each year.

Patient compliance and lifestyle choices Treating or preventing a health condition can be as easy as taking a few pills a day. However, though precise statistics are difficult to determine health experts estimate that perhaps half of people for whom doctors prescribe regular medications do not take them as directed. They may miss doses, combine drugs to consolidate dosages, take a reduced dose to "stretch" the prescription, or take the drug only when they feel symptoms. In some

situations, however, taking a drug improperly is more of a health hazard than not taking the drug at all. The problem is significant enough to support a thriving secondary market that sells various "medication minder" methods. Unfortunately thousands of Americans require additional medical care for circumstances, including unintentional OVERDOSE, that develop as a consequence of failing to follow label instructions.

Health experts also worry that medications are becoming substitutes for healthful changes in lifestyle habits. For example, people who take drugs such as lipid-lowering medications may become complacent about making lifestyle changes that would allow them to stop taking the medication while reducing their risk for cardiovascular disease. Often it is easier to take the pill rather than to change EATING HABITS and exercise habits, another method for lowering blood lipid levels.

Antibiotic resistance The first antibiotics, sulfa and penicillin, became lifesavers during and after World War II. Antibiotics put a rapid end to the often deadly infections rampant at the time, such as PNEUMONIA, TONSILLITIS, GONORRHEA, and TUBERCULOSIS. Within 25 years, however, infections began to appear that were resistant to penicillin, the most commonly used antibiotic, and doctors had to prescribe newly developed alternatives.

ANTIBIOTIC RESISTANCE emerged as a full-blown health issue in the latter decades of the 20th century with the appearance of multiple-drug-resistant infections of tuberculosis, gonorrhea, and pneumonia. By 2002 some strains of *Staphylococcus aureus,* a BACTERIA family accountable for a wide range of infection, including pneumonia and wound infections, had acquired resistance even to the most powerful antibiotic available, vancomycin. Of the most critical concern are NOSOCOMIAL INFECTIONS, infections that result from exposure to bacteria that thrive in environments such as hospitals and extended-care facilities. These bacteria have often evolved to a high level of multiple-drug resistance, making the infections they cause very difficult to treat.

Interactions among drugs An estimated 30 million Americans take multiple prescription medications. Though these drugs keep potentially disabling or deadly health conditions in check, the risk for serious drug interactions increases exponentially with each additional drug. Factor in OTC drugs and herbal remedies, and drug interactions become more likely than not to occur. Such interactions can result in reduced or potentiated effectiveness of any or all of the drugs the person is taking. Doctors and pharmacists urge people always to tell each doctor who provides care, whether or not the doctor writes a prescription, about all drugs they are taking because sometimes the health problems that send them to the doctor result from interactions among their medications.

Breakthrough Research and Treatment Advances

Pharmaceutical research began to focus on pharmacogenomics—the interactions between genetics and medications—in the 1990s. Doctors have known for quite some time that some people metabolize certain drugs more or less efficiently than do other people. This can result in altered efficacy. Researchers have been able to identify genes, some of which regulate CYTOCHROME P450 (CYP450) ENZYMES, the collective of enzymes that metabolize most drugs that enter the body. Subtle differences in protein encoding may slow or speed drug absorption, METABOLISM, or length of time in the BLOOD circulation. Particularly in areas such as cancer treatment, researchers are searching for ways to use pharmaceuticals to manipulate genetic encoding. Other research focuses on developing "smart" drugs, which specifically and narrowly target certain kinds of cells.

A

adverse drug reaction An undesired, negative, and often unpleasant response to a medication. People commonly refer to adverse DRUG reactions as side effects, which is not entirely accurate because a SIDE EFFECT may have therapeutic value whereas an adverse drug reaction is potentially harmful. Adverse drug reactions are common, affecting more than two million Americans each year. They can occur with any drug a person takes or uses, ranging in severity from upset STOMACH or HEADACHE, which often subside after taking the drug for several doses, to URTICARIA (hives) or ANAPHYLAXIS (life-threatening closure of the airways), which are usually allergic reactions. RASH and itching are also common adverse reactions. Adverse drug reactions may also affect the composition of the BLOOD or the function of organs such as the HEART, LIVER, and KIDNEYS.

Intentional misuse of a DRUG, including taking more than recommended or in combination with other drugs, increases the likelihood of adverse drug reaction.

All drugs have some identified potential adverse reactions. These are the events that usually surface during the human testing phase of clinical research studies. Some such reactions may be inherent to the properties of the drug—that is, result from the drug itself. Many ANTIBIOTIC MEDICATIONS, for example, kill BACTERIA in the intestines at the same time they kill bacteria that are causing INFECTION, resulting in DIARRHEA because intestinal bacteria are essential for proper digestion. NAUSEA, VOMITING, and HAIR loss are known adverse reactions with CHEMOTHERAPY drugs. Other such reactions may result from DRUG INTERACTIONS with other medications the person is using or from the ways in which the body responds to the drug over the long term. Tardive DYSKINESIA is a known adverse reaction to long-term use of ANTIPSYCHOTIC MEDICATIONS, for example. Long-term use of CORTICOSTEROID MEDICATIONS, such as taken to treat INFLAMMATORY BOWEL DISEASE (IBD) or ADDISON'S DISEASE, have numerous adverse effects on the body.

Adverse drug reactions may be localized, such as DERMATITIS, or systemic (involve multiple body systems). Doctors generally classify adverse drug reactions as immunologic (those that involve an IMMUNE RESPONSE) or nonimmunologic (those that do not involve an immune response). People who are IMMUNOCOMPROMISED (such as those who have HIV/AIDS or take IMMUNOSUPPRESSIVE THERAPY), have an autoimmune disorder such as RHEUMATOID ARTHRITIS or SYSTEMIC LUPUS ERYTHEMATOSUS (SLE), have liver or kidney disease, take multiple medications (often called polypharmacy), or are age 60 or older have increased risk for adverse drug reactions. Most drug reactions occur within several days to three weeks of beginning the drug, though some long-term adverse reactions occur up to years after the drug's initiation.

COMMON ADVERSE DRUG REACTIONS

allergic response	ANAPHYLAXIS	ANEMIA
ANGIOEDEMA	ARRHYTHMIA	arthralgia
CANDIDIASIS	DERMATITIS	DIARRHEA
GLOMERULONEPHRITIS	LYMPHADENOPATHY	NEUTROPENIA
PRURITUS	RASH on trunk	tardive DYSKINESIA
TINNITUS	URTICARIA	VOMITING

It is important, when beginning treatment with a new medication or adding a different drug to a treatment regimen, to know the expected results and possible adverse reactions. People who take multiple drugs, including OVER-THE-COUNTER (OTC)

DRUGS and MEDICINAL HERBS AND BOTANICALS, should make sure the prescribing physician and the dispensing pharmacist know all of them. Numerous products interact with one another in ways that alter their effects in the body, increasing the risk for adverse drug reactions.

Many countries have regulatory requirements for documenting and reporting adverse drug reactions. Such requirements help oversight agencies and health-care professionals monitor issues with drugs that may not have been apparent during preapproval testing. In the United States the US Food and Drug Administration (FDA) oversees compliance with these requirements and works with pharmaceutical manufacturers to resolve issues that arise.

See also ALCOHOL INTERACTIONS WITH MEDICATIONS; AUTOIMMUNE DISORDERS; CIRRHOSIS; DRUG INTERACTION; LIVER FAILURE; OFF-LABEL USE; RENAL FAILURE; TOXIC EPIDERMAL NECROLYSIS.

aging, effects on drug metabolism and drug response Many drugs have different therapeutic effects as well as potential adverse DRUG reactions, depending on a person's age. The very young and the very old often have limited LIVER function, which affects the ways in which the liver metabolizes drugs, resulting in lower thresholds for toxicity and unpredictable therapeutic effects. In the infant and young child, the liver has not yet fully developed and lacks the structural capacity to metabolize certain substances. The elderly may lose liver function due to CIRRHOSIS, fatty deposits accumulating within the liver (STEATOHEPATITIS), or the normal loss of cells that occurs with aging. Reduced kidney function may further affect drug response by slowing clearance of the drug from the body and thus maintaining higher than expected concentrations of the drug in the BLOOD circulation.

Drugs in Children

Two significant issues surround medication therapy in children. The first is the continually changing metabolic capability and status of the child's body as organ systems grow and mature. The liver remains relatively unsophisticated in its function until a child reaches age 10 or 12 years. Not only does this limit the liver's ability to metabolize drugs such as antibiotics and analgesics (pain relievers), the most common kinds of drugs children may need, but also it makes the liver vulnerable to damage from substances that enter the blood circulation. Incompletely metabolized drugs increase the risk for damage to other developing organ systems as well, notably the CENTRAL NERVOUS SYSTEM. These factors become of therapeutic concern when treating serious childhood diseases for which medications are the primary course of treatment, such as SEIZURE DISORDERS, CONGENITAL HEART DISEASE, and cancer.

The second issue in regard to medication therapy in children is that many drugs do not undergo testing or evaluation for their effectiveness or safety in pediatric use because children make up a very small percentage of the drug's intended patient population or because the potential risks of involving children in clinical research studies are too high. The consequence is that doctors rely on best practices standards and OFF-LABEL USE of drugs in prescribing medications, which are safe and effective in adults but untested in children, to treat health conditions in children.

Drugs in the Elderly

The body undergoes significant metabolic and functional changes by the seventh and eighth decades of life, a blend of the normal processes of aging and the cumulative effect of health conditions. The liver and KIDNEYS become less efficient, which affects the amount of a drug that enters the blood circulation and how long the drug remains in the body. Health conditions such as ATHEROSCLEROSIS (fatty deposits in the walls of the arteries) may alter the flow of blood through the body. Changes in NERVOUS SYSTEM function may alter the release of neurotransmitters. These kinds of changes in the body influence how, and how well, drugs work.

Often the very reasons elderly people need to take therapeutic drugs (such as to treat CARDIOVASCULAR DISEASE [CVD], DIABETES, kidney disease) have significant effects on the ways in which the body can handle the drugs and how those drugs affect the body. As well, older people are more likely to have complex or multiple health conditions and take multiple medications, increasing the risk for ADVERSE DRUG REACTION, DRUG INTERACTION, and OVERDOSE.

See also APOPTOSIS; NEUROTRANSMITTER; ORPHAN DRUG.

antibiotic resistance The adaptation of bacterial strains to certain of the ANTIBIOTIC MEDICATIONS doctors prescribe to treat infections the BACTERIA cause, rendering the antibiotic ineffective. Such adaptation is an evolutionary mechanism that allows the strain of bacteria to survive. Though in most situations the strain of bacteria remains sensitive to other antibiotics even as it develops resistance to a particular antibiotic, antibiotic resistance is a very serious concern in modern health care because the more common strains of bacteria are developing broad bases of resistance to multiple antibiotics. A few strains have mutated to resist all available antibiotics, presenting a worrisome challenge for fighting the infections they cause.

Bacteria, Infection, and Antibiotics

Bacteria are single-cell microorganisms that exist in broad families with numerous strains, or variations, within the same family. Under supportive circumstances each individual strain can cause unique and specific infections. Most bacteria that cause INFECTION in people are normally present in the body and the environment. Ordinarily these bacteria are harmless or even beneficial to body functions, such as the bacteria in the gastrointestinal tract that aid in digestion. NORMAL FLORA bacteria become pathogenic when there is a breach, such as a wound, in the body's protective mechanisms, or when something goes awry with the body's balance of microorganisms and the IMMUNE SYSTEM cannot keep bacterial growth in check.

Antibiotics kill bacteria, either by direct toxicity to the bacteria or by preventing the bacteria from reproducing. Antibiotics are effective for treating only *bacterial* infections; they cannot treat viral infections. Chronic conditions such as BRONCHITIS and OTITIS media (middle EAR infection) are often viral, yet are among the top ailments for which doctors prescribe antibiotics. It is not possible to determine the cause of an infection by evaluating the symptoms, though certain characteristics make it more likely that an infection is bacterial. Only a laboratory culture of cells from the infection, in which cells of a bacterial strain may or may not grow in the lab, can identify the cause of an infection as bacterial.

How Bacteria Acquire Resistance

Bacteria reproduce rapidly, which gives them the opportunity to change rapidly. Over multiple generations the bacteria's DNA—its GENETIC CODE—mutates to establish adaptations beneficial to the bacterial strain's survival. These adaptations include increased resistance to the antibiotics that people take to fight the infections the strain causes. Bacteria generally mutate through one of three processes:

- Spontaneous MUTATION is when changes occur within the DNA alter the bacteria's adaptive ability across the bacterial strain. Resistance due to spontaneous mutation, also called evolutionary mutation, develops over multiple generations of the bacterial strain.
- Transformation is when the DNA from resistant bacteria enter another bacteria that are not yet resistant. Also called DNA uptake, transformation expedites the mutation process to allow bacterial strains to become more rapidly resistant than they would through spontaneous mutation.
- Plasmid transfer is when plasmids (molecules that contain incomplete fragments of genetic material) move among different kinds of bacteria. Plasmids impart limited genetic encoding related primarily to the survivability of a bacterial strain and can result in rapid adaptation to produce antibiotic resistance. Because antibiotic resistance has become a key purpose of plasmid transfer, researchers designate such plasmids as R plasmids.

Resistance resulting from spontaneous, or evolutionary, mutation is the most common adaptation process and accounts for most of the resistant strains of GONORRHEA and *Staphylococcus aureus* infections. Transformation, or DNA uptake, is a more sophisticated, biologically intentional process than spontaneous mutation. Among the three mutation processes plasmid transfer is the most efficient and creates the greatest concern in regard to antibiotic resistance. Plasmids can transfer among different strains of bacteria within a bacterial family, sharing

adaptive mutations for multiple resistance. Plasmid transfer accounts for resistance to entire classifications of drugs such as the quinolones, a family of antibiotics that attack enzymes that facilitate DNA cleavage (the division of DNA in preparation for cell reproduction) in bacteria.

Factors That Contribute to Antibiotic Resistance

Antibiotic use itself is the precipitating factor for the adaptive changes that occur in bacteria to result in antibiotic resistance, as these changes represent natural survival efforts. Key circumstances that further encourage survival adaptations include the following:

- Inappropriate prescribing of antibiotics for infections that are viral or of uncertain cause. The US Centers for Disease Control and Prevention (CDC) believes about half of the 100 million antibiotic prescriptions US doctors write each year are unnecessary because the conditions they are treating are not bacterial.
- Failing to complete the full course of antibiotic therapy, which allows some bacteria to escape eradication. It is important to take a therapeutic antibiotic long enough to kill all the bacteria, extending through their complete life cycle, that are causing infection. Bacteria that are exposed to the antibiotic but do not die have the opportunity to undergo adaptive mutation, which results in antibiotic resistance.
- Prophylactic antibiotics given to food animals such as cattle, pigs, and chickens to prevent them from getting infections that slow their growth. The constant exposure to the same antibiotics fosters adaptive mutation in bacteria that may then become infective agents in people. Humans become vulnerable to infection from resistant bacteria through eating meat from treated animals that is not thoroughly cooked, which allows the bacteria to enter the body. Exposure to the bacteria in environmental settings also is a source of infection.

Limiting Antibiotic Resistance

The most effective measure for reducing antibiotic resistance is to decrease the use of antibiotics. To this end, health experts offer these recommendations for individuals:

- Take antibiotics only for infections that laboratory tests prove are bacterial.
- Take all doses of the antibiotic for the full course of prescribed treatment.
- Wash hands frequently with soap and warm water to prevent the spread of infection-causing bacteria and other pathogens.
- Limit exposure to other people who are ill.
- Choose meat and poultry products that are labeled antibiotic free.

Health experts also are reexamining the practice of ANTIBIOTIC PROPHYLAXIS (administering antibiotics to prevent infection in people who are IMMUNOCOMPROMISED or exposed to risk for NOSOCOMIAL INFECTIONS). The US Food and Drug Administration (FDA), which oversees drug approval and prescribing practices in the United States, issued new regulations in 2003 that establish stringent criteria for doctors to follow in prescribing antibiotics and is spearheading public education efforts to improve public awareness of antibiotic resistance.

See also BACTEREMIA; FOOD SAFETY; HAND WASHING; OPPORTUNISTIC INFECTION; PATHOGEN; PERSONAL HYGIENE.

antitoxin A serum product, cultivated from animal (usually horse) BLOOD, that counteracts the effects of toxins (poisons) certain strains of anaerobic BACTERIA produce when they enter the body. The antitoxin binds with the toxin that is circulating in the bloodstream, neutralizing it. Some antitoxins, such as those for *Clostridium tetani* (tetanus) and *Corynebacterium diphtheriae* (DIPHTHERIA), are effective prophylactically (administered to prevent illness); doctors administer these as vaccines. Others are effective therapeutically; doctors administer them when exposure triggers illness, such as to *Clostridium botulinum* (BOTULISM). Antitoxins for tetanus and diphtheria also have therapeutic action in people who develop these conditions. About 10 percent of people have allergic reactions to antitoxins. Giving smaller amounts of the antitoxin over a longer period of time, such as when treating disease, often mitigates the reaction.

See also ANTIVENIN; CHILDHOOD DISEASES; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS; VACCINE.

antivenin A serum product, also called antivenom, cultivated from animal BLOOD and given therapeutically to neutralize the effects of poisonous venoms such as from BITES AND STINGS. Antivenin is specific to a particular venom and works by activating antibodies that enable the person's IMMUNE SYSTEM to fend off the effects of the venom.

When possible, safely capture the snake or spider that renders the bite for positive identification and the correct antivenin.

A person generally must receive antivenin within about four to eight hours of the bite or sting for the antivenin to be effective. Antivenin is commonly available in the United States for the bites of indigenous snakes and spiders and the stings of scorpions. There are facilities in many parts of the United States that stock antivenin for exotic snakes and spiders that may enter the country inadvertently (such as among produce), as pets, or for scientific research or display (as in zoos). Local and regional poison control centers know what antivenin products are available and how to obtain them.

Most antivenins are cultivated from the blood of horses so it is important to know a person's allergy history. Allergic reaction to antivenin is not uncommon. Even in people who have a known ALLERGY to horses, however, the antivenin may be lifesaving. Generally in such a situation the administration of ANTIHISTAMINE MEDICATIONS and EPINEPHRINE will mitigate the allergic response to allow the antivenin to be effective. Serum sickness, an immune reaction to the antigens and blood proteins present in products derived from nonhuman blood, may also occur. Serum sickness generally begins one to two weeks after administration of the antivenin and runs its course over about three weeks. The risk for allergic reaction and serum sickness increases with higher doses of antivenin.

See also ANTIBODY; ANTIGEN; HYPERSENSITIVITY REACTION.

B–D

bioavailability The amount of a DRUG's active ingredient the body absorbs and the length of time it takes for that ingredient to cause an effect in the body. A common means of determining bioavailability is to measure the concentrations of the drug in the BLOOD circulation or in the URINE at certain time intervals. Doctors know the spectrum of bioavailability and calculate DOSAGE to obtain the desired therapeutic concentration of the drug.

For most drugs the spectrum of activity provides adequate therapeutic levels and tests to measure the drug's concentrations are not necessary. NARROW THERAPEUTIC INDEX (NTI) drugs such as the anticoagulant warfarin, the antiarrhythmic digoxin, and HORMONE supplements such as levothyroxine (thyroid hormone) require diligent assessment and monitoring because the margin between therapeutic and toxic is very close. The doctor may also assess the drug's bioavailability through observation of clinical changes, such as an INFECTION that improves with antibiotic therapy or BLOOD PRESSURE that drops with antihypertensive medications.

For the most part pharmaceutically equivalent drugs (generic drugs) have consistent bioavailability across manufacturers and are interchangeable from this perspective. The exceptions are NTI drugs, for which doctors and pharmacists recommend staying with the same brand name of drug for the duration of treatment. Which brand does not matter so much as that the brand remains consistent. This is because even minute variations in the manufacturing process, as is inherent in different formulations of the same drug product, affect the way the body absorbs and metabolizes the drug. Other factors that influence bioavailability are interactions with foods, other drugs, and MEDICINAL HERBS AND BOTANICALS. Health conditions such as gastrointestinal MALABSORPTION, renal failure, or LIVER FAILURE, as well as the person's age and weight, and metabolic disorders, also affect bioavailability.

See also EFFICACY; GENERIC DRUG; HALF-LIFE; THERAPEUTIC EQUIVALENCE.

bioequivalence A DRUG that has the same biological effect in the body as a substance the body makes naturally (such as a HORMONE supplement) or two or more drugs that have the same BIOAVAILABILITY and EFFICACY. Bioequivalence is a significant concern with NARROW THERAPEUTIC INDEX (NTI) drugs, which require precise and consistent dosing, as well as with generic drugs.

A GENERIC DRUG, which is a different chemical formulation of equivalent active ingredients compared to the innovator (original) drug, is not necessarily bioequivalent to the INNOVATOR DRUG. That is, the same drug product from different manufacturers may contain the same amounts of active ingredient though not the same inactive ingredients or different proportions of inactive ingredients. The extent to which these differences influence bioavailability (the amount of the active ingredient that enters the body) varies among classifications of drugs and is especially crucial with NTI drugs.

The US Food and Drug Administration (FDA) establishes and regulates the parameters of bioequivalence. Drugs that are bioequivalent must fall within a specific range for the amount of time it takes for each drug to enter and remain in the BLOOD circulation.

See also DRUG INTERACTION; *ORANGE BOOK, THE*; THERAPEUTIC EQUIVALENCE.

cytochrome P450 (CYP450) enzymes A group of about 60 endogenous enzymes (enzymes the

body produces) that participate in the METABOLISM of drugs. The CYP450 enzymes also participate in lipid (notably cholesterol) and steroid HORMONE synthesis. Most of the CYP450 enzymes that are active in DRUG metabolism are in the LIVER and the SMALL INTESTINE. The CYP450 enzymes function as catalysts to facilitate the processes by which the drug transforms from its initial chemical structure to the biochemical forms that have action in the body. Each of the CYP450 subtypes, also called isoforms or isoenzymes, metabolizes certain drugs or groups of drugs.

Hormones, antibodies, and foods affect the activity of CYP450 enzymes. Interactions among them may block or enhance a drug's activities; these effects may be beneficial or harmful. Some drug treatment regimens for complex conditions such as HIV/AIDS work by manipulating CYP450 enzyme activity to take advantage of beneficial interactions. Harmful interactions may manifest as adverse drug reactions such as toxicity or unpleasant side effects.

Individuals may express CYP450 activity differently—that is, known variation exists among individuals in the ways CYP450 enzymes function. These variations in CYP450 expression factor into individual responses to medications, at least partially accounting for why one drug may be more or less effective than another drug in the same drug family for a particular individual.

See also ALCOHOL INTERACTIONS WITH MEDICATIONS; ANTIBODY; PHARMACODYNAMICS; PHARMACOKINETICS.

dosage The therapeutic course of a DRUG, encompassing the drug's DOSE (amount of the drug taken), the frequency of the doses, the health condition and status of the person (including age and gender), and the total length of time the drug the person needs to take the drug. For many drugs there are standard dosages that are applicable to most people. The doctor or pharmacist calculates dosages for people who fall outside the standard range, and for NARROW THERAPEUTIC INDEX (NTI) drugs (drugs for which the margin between therapeutic and toxic is very close). People who may fall outside the standard range of dosage for many drugs are the very young, the very old, those who are extremely underweight, those who are extremely overweight, those who have multiple health conditions, and those who take numerous medications.

See also AGING, EFFECTS ON DRUG METABOLISM AND DRUG RESPONSE; PEAK LEVEL; THERAPEUTIC LEVEL; TROUGH LEVEL.

dose The amount of a DRUG a person takes or receives at a single time. A dose falls within a recommended therapeutic range for the drug, the person's condition, and the person's personal health circumstances (including age and gender). An excess of this amount is an OVERDOSE, which can have serious and even fatal consequences.

See also AGING, EFFECTS ON DRUG METABOLISM AND DRUG RESPONSE; DOSAGE; PEAK LEVEL; THERAPEUTIC LEVEL; THERAPEUTIC WINDOW; TROUGH LEVEL.

drug Any product that, when it enters the body, changes the function of the body in some way. Drugs such as ANTIBIOTIC MEDICATIONS work by killing BACTERIA within the body, for example, and antiarrhythmia drugs work by altering the electrical activity of the HEART. As the mainstay of modern medicine, drugs exert therapeutic actions to treat numerous health conditions.

See also ADVERSE DRUG REACTION; ALCOHOL; DRUG INTERACTION; INVESTIGATIONAL NEW DRUG (IND); OFF-LABEL USE.

drug interaction An effect or action that occurs in the body as a consequence of taking two or more drugs that does not occur when taking any one of the drugs alone. Drugs may interact with each other, OVER-THE-COUNTER (OTC) DRUGS and products, vitamin and mineral supplements, MEDICINAL HERBS AND BOTANICALS, and foods. Most DRUG interactions are inadvertent, occurring when a person takes an OTC medication with prescription medications, for example, or when a doctor prescribes a new medication without knowing all of the other medications a person is taking. The latter circumstance becomes a particular challenge when a person must receive urgent care in a clinic, hospital emergency department, or other setting in which the provider is someone other than the person's regular health-care provider.

Some drug interactions are neutral or even beneficial, such as when one medication potentiates (increases or enhances) or mitigates the

action of another in a known and predictable way for a therapeutic effect. Such effect occurs, for example, with the combination of codeine (a narcotic PAIN reliever) and promethazine (Phenergan), an antiemetic medication (reduces NAUSEA). Though an effective pain reliever, codeine tends to cause nausea, but promethazine offsets this effect. And though promethazine alone has no analgesic (pain-relieving) effects it does potentiate, or intensify, the actions of codeine on the CENTRAL NERVOUS SYSTEM as well as mitigate its tendency to cause nausea. Other drug interactions can lessen or intensify the effects of one or more of the involved drugs in ways that are detrimental, either by causing adverse actions in the body or preventing the therapeutic effects of one or any of the drugs. Certain ANTIBIOTIC MEDICATIONS, for example, diminish the effectiveness of oral contraceptives (birth control pills).

It is important for every doctor, dentist, or other health-care provider who prescribes a DRUG for an individual to know all of the drugs, prescription and over-the-counter products (including herbal remedies and natural products) that the person is taking.

Most drug interactions occur as the result of a family of enzymes responsible for drug METABOLISM. These enzymes, called CYTOCHROME P450 (CYP450) ENZYMES, are abundant in the SMALL INTESTINE and the LIVER. CYP450 enzymes in the small intestine initiate the process of metabolism to allow molecules of the drug's active ingredient to pass into the BLOOD circulation. The blood carries the molecules to the liver, where the CYP450 enzymes there complete metabolism. There are numerous subtypes of CYP450 enzymes, each responsible for specific metabolic activity for certain drugs. Some drugs work by inducing and others by inhibiting particular CYP450 enzyme subtypes, which in turn affects the metabolism of other drugs. Other drug interactions may occur when the chemicals the drugs contain interact in some fashion. Iron and calcium in foods, vitamin supplements, and ANTACIDS bind with some antibiotics in the STOMACH, for example, preventing the antibiotic from becoming absorbed and entering the blood circulation.

The potential for drug interaction is extensive. The more medications a person takes, the higher the risk for drug interaction. A useful safeguard is to ask the pharmacist when picking up a prescription what other drugs and foods might interact with it. Even when foods do not directly interact with drugs, they may affect the drug's absorption into the body.

See also ADVERSE DRUG REACTION; ALCOHOL INTERACTIONS WITH MEDICATIONS; ANTIEMETIC MEDICATIONS; CONTRACEPTION; ILLICIT DRUG ABUSE; OVERDOSE; PRESCRIPTION DRUG ABUSE.

COMMON DRUG/DRUG AND DRUG/FOOD INTERACTIONS

This Drug	In Combination with This Drug or Food	Consequence of Interaction
anticoagulant medications (heparin, warfarin)	aspirin GINGKO BILOBA	further decreases clotting response of the BLOOD, raising risk for bleeding
antiplatelet medications (cilostazol, clopidogrel, dipyridamole, ticlopidine)	large quantities of spinach vitamin supplement containing VITAMIN K	increases ability of blood to clot, diminishing effectiveness of ANTICOAGULANT THERAPY
ANTIFUNGAL MEDICATIONS (fluconazole, griseofulvin, itraconazole, ketoconazole)	ALCOHOL of any kind (including in medications such as cold and flu products)	increases the risk for liver failure

This Drug	In Combination with This Drug or Food	Consequence of Interaction
beta blockers (acebutolol, atenolol, betaxolol, bisoprolol, carteolol, carvedilol, esmolol, labetalol, metoprolol, nadolol, penbutolol, pindolol, propranolol, sotalol, timolol)	oral antidiabetes medications	decreases effectiveness of oral antidiabetes medications masks presence of HYPOGLYCEMIA
	H2 blockers	reduces liver's ability to metabolize beta blocker, allowing potentially toxic levels to accumulate in the blood circulation
	MAOI antidepressants	increases MAOI level; high risk for toxicity
	cigarette smoking	reduces effectiveness of beta blocker
H2 ANTAGONIST (BLOCKER) MEDICATIONS (cimetidine, famotidine, ranitidine, nizatidine)	antifungal medications	reduces absorption and effectiveness of antifungal medications
	oral antidiabetes medications INSULIN	increases effectiveness of antidiabetes medications, raising risk for hypoglycemia
	beta blockers	increases effectiveness of beta blockers, raising risk for bradycardia and HYPOTENSION
	tricyclic antidepressants (amitriptyline, desipramine, imipramine, nortriptyline)	increases antidepressant level in blood circulation, raising risk for serotonin syndrome
metronidazole (Flagyl)	alcohol of any kind (including in medications such as cold and flu products)	action similar to that of disulfiram (antabuse)
	lithium	lithium toxicity
	anticoagulant and antiplatelet medications	further decreases clotting response, raising the risk for bleeding
monoamine oxidase inhibitor (MAOI) ANTIDEPRESSANT MEDICATIONS (isocarboxazid, phenelzine, selegiline, tranylcypromine)	beta blockers foods high in tyramine (beer, red wine, processed cheeses, smoked meats, avocados, bananas, raisins, cured foods) GINSENG CAFFEINE in beverages or medications	sudden, rapid, and very high surge in BLOOD PRESSURE (potentially fatal)

This Drug	In Combination with This Drug or Food	Consequence of Interaction
oral antidiabetes medications	alcohol	decreases effectiveness of oral antidiabetes medication
	CORTICOSTEROID MEDICATIONS thiazide diuretics aspirin and other salicylates MAOI antidepressants NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) sulfonamide antibiotics warfarin	increases effectiveness of oral antidiabetes medication
quinolone antibiotics (ciprofloxacin, levofloxacin, ofloxacin, trovafloxacin) tetracycline antibiotics (doxycycline, minocycline, tetracycline)	ANTACIDS dairy products calcium supplements iron supplements	chemical binding in stomach prevents absorption of antibiotic
beta-hydroxy-beta methylglutaryl–coenzyme A (HMG-CoA) reductase inhibitor (statin)	grapefruit juice	decreases liver's ability to metabolize statins
	antibiotic and antifungal medications	various adverse reactions
lipid-lowering medications (atorvastatin, fluvastatin, lovastatin, pravastatin, simvastatin)	oral contraceptives (birth control pills)	reduced effectiveness of the oral contraceptive

E–I

efficacy The ability of a DRUG to produce a predictable effect in the body. Many factors influence a drug's efficacy, from foods and other drugs to health conditions and a person's metabolic characteristics. An individual's age, weight, gender, and level of activity also may affect the rate at which a drug enters, and how long it stays in, the BLOOD circulation. Efficacy is a key factor in determining a drug's potential effectiveness to treat a particular condition in a specific individual. Some drugs have greater efficacy in younger people, for example. Other factors that are also relevant include BIOAVAILABILITY and BIOEQUIVALENCE.

See also CYTOCHROME P450 (CYP450) ENZYMES; THERAPEUTIC WINDOW.

formulary A list of the prescription drugs a health plan or insurance company, including state and federal health insurance programs, will cover. Typically a committee of physicians and pharmacists makes the determinations about what drugs appear in the formulary and why. Factors for consideration include

- the DRUG'S EFFICACY
- whether generic products are available
- similarity to other drugs that are less expensive or have fewer side effects
- NARROW THERAPEUTIC INDEX (NTI) status
- the need for the drug within the insurer's patient population
- whether over-the-counter forms of the drug are available
- the drug's approved uses

Most insurers update their formularies at least annually. An insurer may pay a smaller percentage of the cost for a nonformulary drug or may choose not to cover (pay for) nonformulary drugs at all except within the parameters of specifically defined criteria. A doctor may prescribe a drug that is not on the formulary even though the insurer may refuse to pay for it. The person may still receive the drug by paying for the prescription. Drug formularies help establish consistent prescribing practices as well as control costs for the insurer.

See also GENERIC DRUG; *ORANGE BOOK, THE*; OVER-THE-COUNTER (OTC) DRUGS; PHARMACOPEIA; SIDE EFFECT.

generic drug A DRUG that has BIOEQUIVALENCE and THERAPEUTIC EQUIVALENCE to its INNOVATOR DRUG (the first drug to receive approval for use). Generic drugs became significant in the health-care industry in the 1970s when manufacturing requirements and procedures became standardized and patents began to expire on innovator drugs, converging factors that opened the market for competition within the pharmaceutical industry. Most generic drugs are significantly less expensive than their innovator counterparts, and most states have laws allowing pharmacies to substitute generic drugs when filling prescriptions unless the prescribing provider specifies otherwise. The intent behind such laws is to provide consumers with cost-effective alternatives for prescription drugs. Generic products are also available for many OVER-THE-COUNTER (OTC) DRUGS, allowing consumers to choose either generic or trade name products.

The US Food and Drug Administration (FDA), the federal regulatory agency that approves drugs for use in the United States, establishes the criteria for potency, purity, consistency, and efficacy all drugs must meet. These criteria are the same for

innovator and generic drugs. Generic drugs may also have trade names, which manufacturers often use to establish brand recognition and brand loyalty for marketing purposes. For example, Elavil and Endep are trade names for amitriptyline, a commonly prescribed tricyclic antidepressant. The manufacturer of an innovator drug may also produce and market generic versions of the drug when the innovator drug's patent expires.

In nearly all circumstances a person may take any manufacturer's product, generic or innovator drug, and experience the same therapeutic effects. The only exception is with NARROW THERAPEUTIC INDEX (NTI) DRUGS, in which the margin between the therapeutic dose and the toxic dose is exceedingly small. People who take NTI drugs should always take the same product, whether the innovator drug or a generic drug. Variations in the drug's inactive ingredients can affect how the body absorbs the drug, which can have therapeutic significance with NTI drugs.

In its electronic document *THE ORANGE BOOK*, the FDA maintains a list of newly approved generic drugs, updated each month, and a list of all generic drugs available in the United States. *The Orange Book* is available at the FDA's Web site (www.fda.gov/cder/ob).

See also INVESTIGATIONAL NEW DRUG (IND); LEGEND DRUGS; OFF-LABEL USE; SCHEDULED DRUG.

half-life The length of time it takes for the body to metabolize or eliminate from the body 50 percent of the amount of a DRUG a person takes or receives. Drug half-life is an important factor in determining appropriate DOSAGE and for treating OVERDOSE. Drug half-life also helps the doctor know when to expect to begin to see the effects of the drug. The calculation of drug half-life is logarithmic. Drug informational literature, packaged with prescription drugs, provides general information about the drug's half-life that is generally adequate for most clinical circumstances. A doctor may conduct BLOOD tests to measure the levels of a drug in an individual's blood circulation over a period of time as a means of indirectly assessing half-life, though this is seldom therapeutically necessary.

See also BIOAVAILABILITY; CYTOCHROME P450 (CYP450) ENZYMES; EFFICACY; METABOLISM; PEAK LEVEL; THERAPEUTIC LEVEL; THERAPEUTIC WINDOW; TROUGH LEVEL.

imported drug A DRUG or pharmaceutical product not manufactured in the country of purchase. Countries may have differing requirements for testing and product safety for the manufacture and distribution of drugs within their borders. In the United States the Food and Drug Administration (FDA) has regulatory authority over drug production and distribution and establishes the standards for bringing drugs into the country.

The Internet has dramatically broadened access to foreign markets for drugs. Many Americans are drawn to Internet purchasing because of the ease and convenience and because imported drugs are often less expensive than the same drugs purchased in the United States. However, health experts caution that drugs purchased through locations in other countries, either by mail order or via the Internet, may not meet US quality standards for purity, potency, and safety and may not be legal to bring into the country.

The FDA supports the National Association of Boards of Pharmacy's Verified Internet Pharmacies Web site, www.nabp.net. This system provides another way for consumers to verify the legitimacy of online pharmacies.

See also GENERIC DRUG; INVESTIGATIONAL NEW DRUG (IND).

innovator drug The first DRUG containing its specific active ingredients to receive approval for use from the US Food and Drug Administration (FDA). An innovator drug's patent protects the drug from market competition, giving its manufacturer exclusive right to produce and sell the drug. The innovator drug's manufacturer generally has invested significant time and money in the drug's development, testing, and approval process. Only when the patent expires may competing pharmaceutical manufacturers produce and market a generic version of the innovator drug.

See also GENERIC DRUG; INVESTIGATIONAL NEW DRUG (IND).

investigational new drug (IND) A new DRUG in the final phases of development for which the US Food and Drug Administration (FDA) grants

restricted approval for use in clinical testing, emergency treatment, or transportation across state lines. Typically the use of an IND must meet one of three requirements:

- The person to receive the IND enrolls in a clinical research study that is evaluating the drug's effectiveness, benefits, and risks among the drug's intended patient population.
- The person to receive the IND has a serious or life-threatening condition the IND is being developed to treat, and there are no ongoing clinical research studies in which the person can enroll.
- The person to receive the IND has a serious or life-threatening condition the IND is being developed to treat, and the FDA is in the process of reviewing the drug's clinical research data.

The most commonly used INDs are antibiotics used to treat multiple-drug-resistant infections and drugs to treat cancer. On its Web site the FDA maintains lists of current INDs by type of drug and information about how to gain access to unapproved drugs (www.fda.gov).

See also ANTIBIOTIC RESISTANCE; OFF-LABEL USE; ORPHAN DRUG.

L–N

legend drug In the United States, any DRUG that requires a physician or other appropriately licensed health-care provider (such as a dentist, optometrist, or podiatrist) to write a prescription and a pharmacist to dispense the medication. The federal approval and regulatory process determines which drugs are legend drugs, the labels of which must carry the admonition, "Caution: Federal law prohibits dispensing without a prescription." Each state further regulates the prescribing and dispensing of legend drugs, though practices are fairly consistent across states. Such regulation includes the kind of information that must appear on the dispensing label and the manner in which the pharmacist must discuss the drug's intended benefits and potential risks with the person receiving the medication. It is common to refer to legend drugs simply as prescription drugs.

See also OFF-LABEL USE; OVER-THE-COUNTER (OTC) DRUGS; SCHEDULED DRUG.

low-cost prescription programs Need-based programs, usually under the sponsorship of major pharmaceutical manufacturers, that make certain prescription medications available to people who lack insurance coverage for prescription medications or who cannot otherwise afford to obtain them. Most low-cost prescription programs have income limitations for enrollees and many require that a doctor refer the person and that the person receive the medications through delivery to the doctor's office. Doctors, hospitals, and pharmacies maintain information about current programs and their enrollment requirements.

Some organizations, such as the American Association for Retired Persons (AARP), also have membership prescription programs that make drugs available to members at a significant discount from regular retail prices. Doctors' offices and clinics hospitals also often have drug samples that pharmaceutical representatives leave. Some programs offer prepaid prescription cards and other kinds of membership promotions for people who do not have insurance to cover prescription drugs but exceed the income levels for low-cost prescription plans. Whether these programs truly save money on prescription drugs depends on the amount and kinds of prescription drugs an individual takes.

See also HEALTHY PEOPLE 2010; ORPHAN DRUG.

narrow therapeutic index (NTI) A very close margin between the concentration in the BLOOD circulation of a DRUG that is therapeutic and the concentration that is lethal (deadly). Pharmacists generally express the therapeutic index as a ratio between the median effective DOSE (ED50) and the median lethal dose (LD50). A drug has a narrow therapeutic index when there is less than a twofold difference between the ED50 and the LD50. With NTI drugs even very small changes in the dose, variations in product potency, or changes in the person's health status can result in toxic levels of the drug with harmful or fatal consequences.

The current standard of practice is to maintain the course treatment with the same drug product rather than substituting across brand and generic products as commonly and safely occurs with non-NTI drugs. Some doctors prefer to use specific brand name products when prescribing NTI drugs. Some states mandate a nonsubstitution standard via law or regulatory code, requiring pharmacies to dispense the original drug product. Some clinical studies support such caution though others suggest that, at least with some NTI drugs, generic

substitution maintains therapeutically acceptable consistency for potency and EFFICACY.

The current standard of practice calls for close monitoring of blood concentrations until the drug reaches the desired therapeutic level, with routine blood tests to monitor blood concentration over time, when the person begins taking a new drug, and when there is a change in the person's health status (including significant change in body weight). Once the blood concentration of the drug reaches a steady state with the drug at a therapeutic level the NTI becomes less of a concern.

COMMONLY PRESCRIBED NARROW THERAPEUTIC INDEX (NTI) DRUGS

aminophylline	carbamazepine	clindamycin
clozapine	cyclosporin	digoxin
disopyramide	isoproterenol	levothyroxine
lithium	metaproterenol	phenytoin
prazosin	primidone	procainamide
quinidine	valproic acid	warfarin

See also BIOAVAILABILITY; BIOEQUIVALENCE; *ORANGE BOOK, THE;* PEAK LEVEL; THERAPEUTIC LEVEL; THERAPEUTIC WINDOW; TROUGH LEVEL.

off-label use Taking a DRUG for a purpose other than that for which it has received regulatory approval. In the United States the Food and Drug Administration (FDA) requires pharmaceutical manufacturers to demonstrate the safety and efficacy of a drug before approving it for use. Once a drug receives FDA approval, however, doctors may legally prescribe it for uses that are consistent with current standards of care. The FDA does not regulate how doctors prescribe or individuals take approved drugs.

Additional beneficial effects of a drug often emerge after the drug has been in use for some time and doctors begin to notice those effects. For some of these drugs the additional effects are so significant that prescribing the drug for them subsequently becomes an approved use. In other situations the drug becomes widely known for its additional effects but the manufacturer does not conduct further studies or seek FDA approval for them.

Off-label use is most common when treating conditions for which conventional therapies are limited or unsuccessful, especially when the condition is progressive or chronic such as MULTIPLE SCLEROSIS, PARKINSON'S DISEASE, CANCER, and CHRONIC PAIN syndromes. Doctors may also turn to off-label use when prescribing medications for children because many drugs receive approval without having been tested for safety and EFFICACY in children. A doctor's decision to prescribe a drug off-label draws from available clinical study results, clinical observations, and best practices standards. It is important for a person considering off-label use of a drug to fully understand the potential benefits and risks of such use as well as the drug's possible side effects and adverse reactions.

See also ADVERSE DRUG REACTION; INVESTIGATIONAL NEW DRUG (IND); SIDE EFFECT.

Orange Book, The A document the US Food and Drug Administration (FDA) maintains that lists all the drugs, prescription and over-the-counter, that have FDA approval for use in the United States. As of 2005 *The Orange Book* is available only as an electronic document (www.fda.gov/cder/ob) on the FDA's Web site (print editions are no longer obtainable). An individual may download the document in a printable format to produce a paper copy, if desired.

The FDA updates *The Orange Book* daily. These updates provide, among other kinds of information, the most current information about newly approved generic products. *The Orange Book* lists drugs by proprietary (trade or brand) name, active ingredient, and patent holder. Listings identify the INNOVATOR DRUG (first drug that received approval) and any GENERIC DRUG also approved for use as well as provide information about the status of the product's patent.

See also FORMULARY; INVESTIGATIONAL NEW DRUG.

orphan drug A DRUG to treat a rare condition. The US Orphan Drug Act of 1983 (ODA) established criteria in the United States to encourage pharmaceutical manufacturers to investigate new drugs and continue to produce approved drugs to treat conditions, such as HUNTINGTON'S DISEASE and some forms of MUSCULAR DYSTROPHY, that affect fewer than 200,000 people. The underlying premise of an orphan drug is that its sales will not generate enough revenue for its manufacturer to recover the costs of its development and testing, a circumstance that makes research and production

unappealing to pharmaceutical manufacturers. The ODA establishes mechanisms of financial support for pharmaceutical manufacturers through grants and tax relief, in return for which the manufacturer agrees to produce and market the drug. Additional grants are available to support research about rare diseases. In 2005 there were approximately 1,400 drugs with orphan drug status. The US Food and Drug Administration (FDA) Office of Orphan Products Development (OOPD) oversees orphan drug research.

See also INVESTIGATIONAL NEW DRUG (IND); OFF-LABEL USE.

outdated drug A DRUG that is past the manufacturer's listed expiration date. An outdated drug may be less effective than the unexpired product or may be harmful. Drugs deteriorate over time. Some drugs have short effective periods, particularly those that require refrigeration. Other drugs maintain potency for years. The US Food and Drug Administration (FDA) requires pharmaceutical manufacturers to determine the length of time a drug remains at full potency and to incorporate an expiration date into the drug's labeling information. In general, pharmacists recommend not using a drug after one year from the date it was opened or removed from its original packaging (including preparation or repackaging as a prescription).

No matter what a DRUG's official expiration date, do not use or take products that are discolored or obviously deteriorated (such as tablets that are crumbling) or when there is damage to the container (such as a crack in a tube or a broken lid).

Factors such as exposure to heat, light, moisture, and air may hasten deterioration, causing a drug to become less effective even before its expiration date. It is important to store drugs in their original or prescription containers and in the appropriate environment. Many people keep medications in a bathroom medicine cabinet, which, though convenient for remembering to take medications at the prescribed times, is a less than ideal environment. Most bathrooms are small and enclosed and experience extreme variations in heat and humidity as a result of people bathing or showering. Pharmacists recommend storing drugs, prescription and over-the-counter, in a cool, dry, dark location unless the label specifies other storage requirements, such as refrigeration.

See also EFFICACY; OVERDOSE.

overdose Consumption of a quantity of a DRUG in excess of its recommended DOSE or of a combination of drugs that results in potentiated effects from any or all of the drugs. Overdose may occur with prescription or OVER-THE-COUNTER (OTC) DRUGS. The consequences of an overdose may range from no apparent symptoms to potentially life-threatening adverse effects. The severity of the consequences depends on numerous factors, including the person's age, health condition, amount and kind of drug, whether the person also consumed ALCOHOL, and to some extent whether the overdose is intentional or unintentional.

Seek immediate medical help for any suspected overdose. Call 911 or the US national poison control hotline at 800-222-1222. Do not induce vomiting unless a health professional so advises. Keep the package or container and any remaining DRUG for positive identification.

Unintentional overdose may occur when a person

- misreads or misunderstands the dosage instructions
- forgets having taken a dose and takes another
- takes one drug thinking it is another drug
- takes multiple drugs that have the same ingredients
- takes a prescription drug and an over-the-counter (OTC) drug that have the same active ingredient
- takes multiple drugs that interact in ways that intensify the effects of one or more of the drugs taken
- drinks alcohol or uses illicit substances when taking the medication

A high risk for overdose exists among young children who spend extended periods of time with older caregivers such as grandparents. Many older people have difficulty with child-resistant drug packaging or set out their medications to remember to take them. Brightly colored tablets and capsules are attractive to young children who think they are candy. The coatings on many pills contain sugar to mask unpleasant flavors during the time the pill is in the person's mouth and to aid in making the pill easy to swallow. A child may experience life-threatening poisoning from taking only a few pills, far fewer than would cause adverse effects in an adult. Medications to treat HEART conditions and iron supplements are among the most hazardous drugs for overdose in children. Overdose of acetaminophen and aspirin may cause permanent LIVER FAILURE or RENAL FAILURE

COMMON DRUG OVERDOSE SYMPTOMS

Type of Drug	Common Symptoms
acetaminophen	initial: NAUSEA, VOMITING, excessive sweating later: ABDOMINAL PAIN, HEPATOMEGALY, JAUNDICE, LIVER FAILURE, RENAL FAILURE
ANTIHISTAMINE MEDICATIONS (brompheniramine, cetirizine, clemastine, diphenhydramine, doxylamine, fexofenadine, loratadine, meclizine, promethazine, tripelennamine, triprolidine)	initial: extremely dry mucous membranes and SKIN, flushing, difficulty urinating, agitation, confusion later: seizures, extreme HYPERTENSION, ARRHYTHMIA, COMA
aspirin, salicylates, and NONSTEROIDAL ANTI-INFLAMATORY DRUGS (NSAIDS)	initial: TINNITUS, vomiting, FEVER, rapid HEART RATE, rapid BREATHING, confusion, HALLUCINATION later: kidney failure, HEART FAILURE, coma, gastrointestinal bleeding
BARBITURATE (pentobarbital, phenobarbital, secobarbital)	initial: drowsiness, lack of coordination, slurred speech, depressed breathing, slow heart rate later: coma, RESPIRATORY FAILURE
BENZODIAZEPINES (alprazolam, chlordiazepoxide, clorazepate, diazepam, flurazepam, lorazepam, oxazepam, prazepam, temazepam, triazolam)	initial: drowsiness, blurred vision, agitation, confusion, hallucinations, depressed breathing, HYPOTENSION later: loss of CONSCIOUSNESS, coma
digoxin	initial: nausea, confusion, blurred vision later: irregular heart beat, CARDIAC ARREST
iron (ferrous gluconate, ferrous fumarate, ferrous sulfate, multiple vitamin and mineral supplement products containing iron)	initial: nausea, vomiting, metallic taste in MOUTH, chills, HEADACHE, dizziness, flushing later: rapid heart rate, hypotension, coma
NARCOTICS (codeine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone)	initial: drowsiness, hypotension, depressed breathing, pinpoint pupils later: respiratory failure
tricyclic ANTIDEPRESSANT MEDICATIONS (amitriptyline, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine)	initial: irregular heart rate, nausea, vomiting, DIARRHEA, hypotension later: seizures, psychotic behavior, arrhythmias, extreme HYPERTENSION, cardiac arrest

requiring LIVER TRANSPLANTATION or KIDNEY TRANSPLANTATION.

Symptoms and Diagnostic Path

The symptoms of drug overdose vary according to the drug or drugs involved and may range from agitation to lethargy to loss of CONSCIOUSNESS. Some symptoms are immediate, such as slowed BREATHING and HEART RATE with narcotic overdose, and others develop over time, such as JAUNDICE, resulting from liver damage. Prompt medical treatment is essential whenever there is cause to suspect overdose. The kinds of symptoms a person has can suggest the general nature of the toxicity (narcotic, cholinergic, hepatotoxic) though it is important to identify as quickly as possible what drug or drugs the person has taken.

Treatment Options and Outlook

Treatment focuses on removing or neutralizing the drug, when health-care providers are reasonably certain what drug or drugs the person has taken. Gastric lavage ("STOMACH pumping") is the common method for attempting to remove ingested (swallowed) drugs. It is effective only within 30 to 60 minutes of ingestion; after this time any swallowed substances have passed from the stomach into the SMALL INTESTINE. Gastric lavage involves inserting a nasogastric tube through the NOSE and down the back of the THROAT into the stomach to withdraw the stomach's contents and flush the stomach with liquid. Sometimes the doctor will infuse a solution of activated charcoal, which is highly absorbent, to help prevent more of the drug from entering the BLOOD circulation. Doctors do not agree about the effectiveness of gastric lavage for improving the person's risk for complications of overdose, and gastric lavage itself carries risks for esophageal perforation (damage to the wall of the ESOPHAGUS) and aspiration of stomach fluids into the LUNGS.

Antagonists, also called antidotes, are available to reverse the effects of some kinds of drugs. They include

- naloxone, which counteracts NARCOTICS
- N-acetylcysteine, which counteracts acetaminophen
- physostigmine, which counteracts some antihistamines
- flumazenil, which counteracts BENZODIAZEPINES

Other treatment targets symptoms and provides supportive care until the body can metabolize enough of the drug for blood concentrations to drop below toxic levels. Such support might include MECHANICAL VENTILATION when breathing is impaired or dialysis for kidney failure. The extent of permanent damage or the likelihood of death depends on the drug and the amount as well as how quickly the person receives treatment.

Risk Factors and Preventive Measures

Child-resistant containers and storing medications in locked cabinets or drawers out of the reach of children are important measures for preventing accidental overdose in children. Adults should store drugs in their original containers and check the container before taking a dose of the drug. Particularly with prescription drugs repackaged in pharmacy containers, it is easy to grab the wrong bottle and take one drug thinking it is another. Contact the pharmacist or doctor if there are unusual symptoms after taking any drug. It is also crucial for the prescribing doctor and the dispensing pharmacist to know all of the drugs a person is taking, prescription and OTC (including MEDICINAL HERBS AND BOTANICALS).

See also ADVERSE DRUG REACTION; AGING, EFFECTS ON DRUG METABOLISM AND DRUG RESPONSE; ALCOHOL INTERACTIONS WITH MEDICATIONS; CYTOCHROME P450 (CYP450) ENZYMES; HEPATOTOXINS; POISON PREVENTION.

over-the-counter (OTC) drug In the United States, a DRUG that is available for purchase without a prescription and that does not require a pharmacist to dispense. However, US laws do require OTC product labels to list the product's active ingredients, main inactive ingredients, strength, recommended DOSAGE, significant side effects (such as drowsiness), and any health conditions a person might have in which the person should not take the drug. Furthermore these drugs must meet drug purity, consistency, and safety standards. OTC drugs are available in a wide variety of retail locations. Most OTC products

come in child-resistant packaging. Tablets and capsules may come in bulk or single-dose packaging.

The US Food and Drug Administration (FDA) oversees the approval of new OTC drugs, which must meet the general criteria that:

- The drug's benefits outweigh its risks.
- A person can take the drug to treat a self-diagnosed condition (such as HEADACHE or seasonal allergies).
- The drug has a low risk for abuse.

Many OTC drugs are lower-dose versions of approved prescription drugs and thus have extensive clinical history that demonstrates their relative effectiveness and safety. Though OTC drugs are generally safe to take without a doctor's oversight of either the drug's use or the condition the person is taking the drug to treat, people who regularly take prescribed or doctor-recommended medications should ask the doctor or pharmacist about possible problems or interactions.

All drugs have potential side effects, adverse reactions, and interactions. OTC drugs may interact with each other or with prescription drugs the person is also taking. Unintentional OVERDOSE may occur when taking a prescription drug and an OTC drug or when taking multiple OTC drugs that contain the same ingredients. This is a particular hazard when taking cold and flu products with ALLERGY relief products, when taking PAIN relief products with cold and flu products, and when taking prescription drugs to treat OSTEOARTHRITIS with pain relievers or cold and flu products. Many cold and flu products contain an antihistamine and an ingredient to relieve pain and FEVER, such as acetaminophen or ibuprofen. Prescription medications for osteoarthritis are often NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS), the same classification of drug as OTC pain relievers such as ibuprofen, ketoprofen, and naproxen. It is important to read product labels carefully and ask the pharmacist about any possible interactions with other medications.

See also ADVERSE DRUG REACTION; ALCOHOL INTERACTIONS WITH MEDICATIONS; GENERIC DRUG; LEGEND DRUG; *ORANGE BOOK, THE*; SCHEDULED DRUG; SIDE EFFECT.

P–S

peak level The maximum concentration of a DRUG in the BLOOD circulation. The peak level corresponds in part to the drug's route of administration, chemical composition, and rate of METABOLISM. A drug's peak level may occur within minutes to several hours of taking or receiving it. Injectable drugs enter the blood circulation rapidly; oral medications (taken by MOUTH) take longer to reach the blood as they must first go through digestion. Foods and liquids also consumed affect the rate of digestion and absorption, as do other factors such as the person's activity level, age, body weight, and any health conditions.

A drug's peak level establishes the upper limit of the drug's therapeutic range. For most drugs it is not necessary for the doctor to determine peak level and TROUGH LEVEL (lowest concentration) as the drug's informational literature provides the expected levels. Improvement in the person's symptoms or condition is clinical evidence that the drug DOSAGE is therapeutically appropriate. The doctor may more closely monitor blood concentrations for NARROW THERAPEUTIC INDEX (NTI) drugs, for which the peak and trough levels are critical. Because the goal of most medication therapy is to achieve a fairly constant level of the drug in the blood circulation, peak and trough levels are primarily significant at the onset of treatment.

See also HALF-LIFE; ROUTES OF ADMINISTRATION; THERAPEUTIC LEVEL.

pharmacodynamics The actions of drugs within the body. Drugs enter and act within the body by binding with cell receptors, specialized fragments of proteins that instruct the cell to take or not take specific actions. This binding process, called selectivity, limits and directs the effects of drugs. Proteins are the basic components of the body's biochemical messengers, hormones and neurotransmitters. The interactions they initiate are often intricate cascades that influence numerous biochemical processes (such as ion passage for cell communication) as well as DNA encoding and transcription (cell function and replication). Numerous factors influence the unfolding of these cascades, from a person's general health status and existing health conditions to other drugs the person is taking. For example, INSULIN RESISTANCE and DIABETES affect the energy accessible to cells to carry out the functions of cellular METABOLISM, altering the processes and outcomes of receptor binding. Through different mechanisms HYPOTHYROIDISM slows and HYPERTHYROIDISM accelerates cellular metabolism, also affecting receptor binding. Pharmacodynamics gives doctors and pharmacists the ability to assess how individuals may react to specific drugs, depending on their unique health profiles.

See also ALCOHOL INTERACTIONS WITH MEDICATIONS; BIOAVAILABILITY; CYTOCHROME P450 (CYP450) ENZYMES; HORMONE; NEURON; NEUROTRANSMITTER; PHARMACOKINETICS.

pharmacokinetics The timing of a DRUG's absorption, METABOLISM, action, and excretion. Pharmacokinetics is an element of DOSAGE determination and the EFFICACY of a drug. Many variables unique to an individual influence the rate of a drug's entry into, stay within, and passage from the body. Mathematical calculations that integrate the drug's characteristics (such as form and strength) with an individual's health circumstances allow doctors and pharmacists to tailor medication therapy regimens specific to the individual's needs.

See also ALCOHOL INTERACTIONS WITH MEDICATIONS; BIOAVAILABILITY; BIOEQUIVALENCE; CYTOCHROME P450 (CYP450) ENZYMES; PHARMACODYNAMICS.

pharmacopeia A professional and regulatory compendium of information about drugs, including their formulations, dosages, and therapeutic uses, that establishes manufacturing, safety, EFFICACY, and prescribing standards. The US Pharmacopeia (USP) is a formal and official document as well as a process for maintaining quality standards across the spectrum of pharmaceutical manufacturers, pharmacies, and health-care organizations (such as practices, clinics, care facilities, and hospitals) after a drug receives approval from the US Food and Drug Administration (FDA). Drugs and products such as dietary supplements that bear the indication "USP-verified" or include "USP" with the product name meet USP standards. Other countries have similar pharmacopeia (commonly spelled "pharmacopoeia" outside the United States) structures.

See also FORMULARY; *ORANGE BOOK, THE*.

placebo An inert substance that has no biological, chemical, or other action within the body, taken with the intent of producing a therapeutic effect. The placebo effect refers to the sense of improvement of symptoms an individual may experience when taking or using a product that has no active ingredients. Researchers often use placebo products when testing new drugs, particularly medications such as PAIN relievers (ANALGESIC MEDICATIONS), in which the assessment of effectiveness has a subjective component.

See also INVESTIGATIONAL NEW DRUG (IND); MIND-BODY CONNECTION.

route of administration The method by which a person takes or receives a DRUG. The common routes administration are oral (by MOUTH), sublingual (beneath the tongue), injection, topical, transdermal, and rectal. Women may use some drugs intravaginally. Some drugs are available only in certain forms, such as injectable. Many drugs are available in numerous forms. Factors that influence the selected route of administration include the drug's formulation and the person's ability to take or receive a particular form of the drug. For example, a young child or person who has difficulty swallowing or is experiencing NAUSEA and VOMITING may better handle a drug adminis-

ROUTE OF DRUG ADMINISTRATION

Route	Forms	Entry Mechanism
injection	intravenous (IV), intramuscular (IM), subcutaneous (SC)	IV: into a VEIN, direct entry to the BLOOD circulation IM: into a MUSCLE; rapid absorption into the blood circulation SC: into the fatty tissue beneath the skin; slow absorption into the blood circulation
oral (*per os* or PO)	tablet, capsule, liquid	digestion breaks down the product, with absorption usually in the SMALL INTESTINE
rectal	suppository	Soft carrier wax melts, drug becomes absorbed into the blood circulation through the wall of the RECTUM
sublingual (SL)	tablet, liquid	dissolves under the tongue, becoming absorbed into the blood circulation through the mucosa of the MOUTH
topical	cream, ointment, gel, lotion, spray	intended to remain within the layers of the SKIN
transdermal	patch, cream, ointment	intended to be absorbed through the skin into the blood circulation

tered by transdermal patch, injection, or rectal suppository. Injection allows the most rapid delivery; other forms allow slower entry of the drug into the BLOOD circulation.

See also BIOAVAILABILITY; PHARMACOKINETICS.

scheduled drug In the United States a DRUG that has strict prescribing and availability criteria because of its potential for ADDICTION or abuse, as the federal Uniform Controlled Substance Act (UCSA) of 1970 specifies and regulates. Some substances are scheduled drugs (also called controlled substances) because they have no medicinal or therapeutic value yet may cause considerable harm or death when used, such as HEROIN and lysergic acid diethylamide (LSD). The UCSA establishes five levels of control for such drugs, indicated by a Roman numeral on the drug package's label.

Each level of control has specific requirements for ordering, storing, prescribing, dispensing, and destroying the scheduled drugs within its definition; in general the distribution system is a closed one in that every individual who handles a scheduled drug must account for that drug's passage through his or her contact. The US Drug Enforcement Agency (DEA) oversees compliance with UCSA regulations. Though state provider licensing regulations designate prescribing authority for scheduled drugs, a provider must have a DEA license to prescribe scheduled drugs.

Schedule I drugs are available only to researchers. Schedule II drugs require a written prescription for each quantity of drug received. Schedule III and schedule IV drugs require a written or oral prescription and are refillable from the original prescription up to five times within six months if the provider authorizes refills. Under federal law schedule V drugs do not require a prescription though states may otherwise regulate their availability.

SCHEDULED DRUGS

Schedule	Common Drugs	Definition
schedule I	HEROIN, LSD, mescaline, methylenedioxymethamphetamine (MDMA), methaqualone, racemoramide, tilidine, trimeperidine	no accepted medical use high risk for abuse unsafe for use
schedule II	amobarbital, AMPHETAMINE, COCAINE, codeine, glutethimide, hydrocodone, hydromorphone, levorphanol, meperidine, METHADONE, methylphenidate, morphine, oxycodone, oxymorphone, pentobarbital	limited medical use high risk for abuse high risk for physical or psychological dependence
schedule III	amobarbital, amphetamine, anabolic steroids, BUPRENORPHINE, chlorphentermine, codeine compounds, GLUTETHIMIDE, hydrocodone compounds, phenmetrazine	accepted medical use moderate risk for abuse moderate risk for physical or psychological dependence
schedule IV	BENZODIAZEPINES, CHLORAL HYDRATE, meprobamate, paraldehyde, pemoline, pentazocine, phenobarbital, propoxyphene compounds, zolpidem	accepted medical use low risk for abuse low risk for physical or psychological dependence
schedule V	codeine COUGH preparations, dihydrocodeine, diphenoxylate	accepted medical use negligible risk for abuse negligible risk for physical dependence, low risk for psychological dependence

See also ILLICIT DRUG USE; LEGEND DRUG; OVER-THE-COUNTER (OTC) DRUGS; PRESCRIPTION DRUG ABUSE.

side effect An action other than the intended therapeutic effect of a DRUG. Side effects may be neutral, beneficial, or harmful. Many side effects are so common as to be expected, such as DIARRHEA with certain ANTIBIOTIC MEDICATIONS (which occurs because antibiotics kill BACTERIA, including the bacteria that normally reside in the gastrointestinal tract to aid in digestion). Some side effects are temporary, such as drowsiness when first beginning treatment with ANTIDEPRESSANT MEDICATIONS (which affect neurotransmitters and functions of the CENTRAL NERVOUS SYSTEM) and NAUSEA at the onset of therapy with antihypertensive medications (which affect the autonomic NERVOUS SYSTEM). A harmful side effect (one that has serious or long-term health consequences) is an ADVERSE DRUG REACTION. It is important to know what side effects can occur with all medications a person is taking, for each individual drug as well as for the drugs in combination with each other. In the United States federal and state laws require product package inserts or label information to contain brief information about possible side effects.

See also ALCOHOL INTERACTIONS WITH MEDICATIONS; DRUG INTERACTION; NEUROTRANSMITTER; OFF-LABEL USE.

T

therapeutic equivalence In pharmacology, drugs that have the same active ingredients in the same forms and have the same actions within the body. The US Food and Drug Administration (FDA), which oversees DRUG approval in the United States, refers to such drugs as bioequivalent with matching EFFICACY and safety profiles. Therapeutically equivalent drugs may have superficial differences such as in appearance (shape or color) and the inactive ingredients that serve as the vehicle to contain the active ingredient. However, they must have the same BIOAVAILABILITY and efficacy.

The FDA has adopted a BIOEQUIVALENCE standard based on a statistical methodology in which the time it takes for each drug to reach its maximum concentration in the BLOOD circulation and the amount of time the drug remains at a THERAPEUTIC LEVEL in the blood circulation differ by no more than 20 percent. In its official listing of approved drugs, *The Orange Book,* the FDA identifies all drugs with alternate products as "A" drugs (therapeutically equivalent) or "B" drugs (not therapeutically equivalent).

Health-care providers other than pharmacists sometimes use the term therapeutic equivalence in the context of different drugs within the same classification that have similar effects—for example the drugs fluoxetine and sertraline, both of which are selective serotonin reuptake inhibitors (SSRIs) to treat DEPRESSION. Though these drugs act in similar ways to achieve a similar therapeutic effect, they do not have the same active ingredients.

See also; GENERIC DRUG; INNOVATOR DRUG.

therapeutic level The amount of a DRUG in the BLOOD circulation that is necessary to achieve and sustain the desired effect for treatment, which is usually a steady state with little variation between the drug's PEAK LEVEL and TROUGH LEVEL. Doctors calculate dosages to achieve a therapeutic level, factoring the person's age, body weight, and other medications with which interactions are possible. For most drugs, blood drawn at any time provides the needed information about the drug's concentration in the blood. At the onset of medication therapy or when taking a drug that has a NARROW THERAPEUTIC INDEX (NTI), blood tests taken to measure both peak and trough levels may provide more useful information to assess whether the drug is at therapeutic level. It often is valuable to tell the doctor or the lab the time of the last DOSE of the medication, which may help to determine whether doses are spaced appropriately.

See also CYTOCHROME P450 (CYP450) ENZYMES; DOSAGE; EFFICACY; THERAPEUTIC WINDOW.

therapeutic window The DOSAGE range within which most of a DRUG's likely population will experience the expected EFFICACY and therapeutic value of the drug. The therapeutic window is important to doctors when they calculate dosages, providing a clinically valid starting point for most people. Individual characteristics such as other health conditions, other medications being taken, body weight, and activity level help the doctor determine where within the therapeutic window is the most appropriate point to choose the starting dosage.

See also PEAK LEVEL; THERAPEUTIC LEVEL; TROUGH LEVEL.

trough level The amount of a DRUG in the BLOOD circulation at the drug's lowest therapeutic concentration. Generally the trough level occurs immediately before the person is due to take the

next DOSE of the drug. The trough level helps the doctor determine if the dosage is appropriate to achieve the desired therapeutic effect and is useful information primarily at the onset of treatment. The goal of most medication therapy is a steady state of the drug's concentration in the body, at which there is little difference between the drug's PEAK LEVEL (highest concentration in the blood circulation) and trough level.

Trough level is an especially important measure for NARROW THERAPEUTIC INDEX (NTI) drugs (drugs for which the margin between therapeutic and toxic is very close) such as theophylline (to treat ASTHMA), certain ANTIBIOTIC MEDICATIONS, cyclosporine for IMMUNOSUPPRESSIVE THERAPY, some antiseizure medications, and many antiarrhythmia medications.

See also HALF-LIFE; THERAPEUTIC LEVEL.

NUTRITION AND DIET

The science of nutrition concerns itself with the ways in which foods influence health and disease. A health-care practitioner who specializes in nutrition may be a registered dietitian (RD), registered nurse (RN), physician (MD or DO), naturopathic physician (ND), pharmacist (RPh or PharmD), or chiropractor (DC). The general term nutritionist is in common use to identify a health-care professional who specializes in matters of nutrition but does not consistently designate specific education, training, qualifications, or credentials.

This section, "Nutrition and Diet," presents an overview discussion of nutritional concepts as they relate to health, health risk factors, and preventive health measures. The entries in this section focus on the broad picture of how nutrition and diet influence health and disease. The section, "Lifestyle: Obesity and Smoking," provides discussion and content of nutritional topics that relate to WEIGHT LOSS AND WEIGHT MANAGEMENT.

Making the Connection between Diet and Health

Though the mechanisms of nutrition remained unknown until the early 20th century, doctors were quite familiar with the diseases of nutritional deficiencies. Ancient Egyptian physicians identified the disease now called SCURVY, which for centuries was the bane of sailors who spent months to years at sea on ships with no fruits or vegetables to supply needed vitamins and minerals. Biscuits and salt pork sustained life but they did not support nutrition. Not until the middle of the 18th century did ships' surgeons recognize that citrus fruits (namely lemons, limes, and oranges) could cure as well as prevent scurvy among sailors.

HEALTH CONDITIONS RESULTING FROM NUTRITIONAL DEFICIENCIES

BERIBERI	MALNUTRITION
NIGHT BLINDNESS	OSTEOPOROSIS
PELLAGRA	pernicious ANEMIA
RICKETS	SCURVY

Among the most famous names in medical nutrition is John Harvey Kellogg (1852–1943), a late-19th-century American physician and surgeon whose belief that diet was the foundation of good health launched what would become one of the world's largest and most successful cereal companies. Kellogg came up with a recipe for a simple, nutritious breakfast food to serve at the sanitarium where he was at the time the director: cornflakes. The product based on the recipe became itself an American institution. Kellogg implemented many practices based on nutrition during his tenure at the sanitarium, gaining prominence for them in a time when other medical alternatives were fairly nonexistent.

In the flood of transforming discoveries sweeping the practice of medicine, diet was not especially exciting and its connections to health unproven. Researchers discovered aspirin, INSULIN, antibiotics, immunizations, and ANESTHESIA. Surgeons invaded the belly, chest, and cranium. Kellogg, himself a talented surgeon, developed a number of surgical techniques and the instruments to carry them out. Though Kellogg's cornflakes became a national phenomenon, doctors did not pay much attention to the role of diet—the kinds and amounts of foods people eat—in health unless they were treating conditions resulting from or that caused NUTRITIONAL DEFICIENCY or toxicity.

About the time John F. Kennedy became US president, researchers established the first diet–disease correlation, that between cholesterol and

CARDIOVASCULAR DISEASE (CVD). Following shortly was the first official recommendation to limit consumption of a particular food, eggs, as an effort to prevent disease. In the decades since, research has confirmed a tight and intricate relationship between DIET AND HEALTH, and diet-related health conditions became the focus of renewed effort to identify nutritious, healthful foods.

HEALTH CONDITIONS LINKED TO DIETARY FACTORS

ATHEROSCLEROSIS	BREAST CANCER
cervical dysplasia	CERVICAL CANCER
COLORECTAL CANCER	CORONARY ARTERY DISEASE (CAD)
DENTAL CARIES	HYPERLIPIDEMIA
HYPERTENSION	OBESITY
PERIPHERAL VASCULAR DISEASE (PVD)	PROSTATE CANCER
STOMACH CANCER	type 2 DIABETES

Current Challenges and Future Directions

A key challenge today is the rapidly changing understanding of the relationships between nutrition and health and between nutrition and disease. Though a general range of nutrient intake is adequate for most healthy adults, it is becoming increasingly clear that individual variations in NUTRITIONAL NEEDS and nutrient intake can make the difference between health and disease. The medical community is in transition in regard to nutritional recommendations, shifting from the system in place since the early 1940s to methods of NUTRITIONAL ASSESSMENT that take individual variations more into consideration. Current research is exploring the ways in which NUTRIENTS may serve to lower health risk factors, such as for CVD and diabetes, over the length of the lifespan.

A

aging, nutrition and dietary changes that occur with Nutritional needs and dietary choices change across the spectrum of age. Diet and nutrition also influence the processes of aging and the status of health.

Food Choices and Lifelong Health

Health experts recommend BREASTFEEDING for infants, in most circumstances, from birth through at least six months of age if possible. Breast milk fulfills 100 percent of an infant's NUTRITIONAL NEEDS, provided the mother is meeting her own nutritional needs, and provides the infant with extended immune coverage until his or her own IMMUNE SYSTEM develops enough to become protective. Infants for whom breastfeeding is not practical or appropriate should receive fortified formulas that meet their nutritional needs. Cow's milk does not provide adequate nutritional value and contains higher amounts of sugars than infant formulas.

The nutritional needs of the toddler and older child focus on supporting proper growth and development. Children who learn to make nutritious food choices, including portion size, early in life are likely to make such choices the mainstay of diet throughout life. Healthy children do not require vitamin or mineral supplements and should take them only when a doctor recommends them.

A critical health problem among children is OBESITY, which sets the stage for a plethora of health challenges that can have lifelong consequences. Researchers are identifying in children, especially teens, diseases formerly the exclusive territory of middle age such as type 2 DIABETES, OSTEOARTHRITIS, and ATHEROSCLEROSIS. Nutritious EATING HABITS are an important component of weight management. However, children should not go on "diets" or have food intake restricted without precise instructions from a doctor or nutritionist.

Health Changes and Nutrition

Beginning in middle age people start to experience physical changes that alter their ability to digest foods and absorb NUTRIENTS. The STOMACH produces less acid, and foods may stay in the stomach longer before being digested enough to progress to the SMALL INTESTINE. The stomach also produces less intrinsic factor, a biochemical essential for the absorption of vitamin B_{12} (cyanocobalamin). Dental conditions and changes to the gums (such as PERIODONTAL DISEASE) may result in lost TEETH and difficulty chewing. Perceptions of taste and smell may change, altering the desire for certain foods. Other changes include a generalized slowing of the metabolic rate, which affects digestion and nutrient absorption, and a decreased need for nutrients (fewer calories).

Health conditions with metabolic consequences, such as diabetes and GALLBLADDER DISEASE, become more prevalent with advancing age. Health conditions for which nutrition plays a role, such as CARDIOVASCULAR DISEASE (CVD), also become more prevalent. Other chronic health conditions may accelerate the body's use of certain nutrients. Both men and women begin to experience changes in BONE DENSITY and BONE mass in middle age, women in an especially pronounced manner after MENOPAUSE. Without proper vitamin D and calcium intake, OSTEOMALACIA and OSTEOPOROSIS are significant threats to bone health.

The very old (80 and older) may have mobility, independence, and economic issues that prevent them from eating appropriately. Debilitating conditions such as ALZHEIMER'S DISEASE, DEMENTIA, and PARKINSON'S DISEASE are more common among the

elderly. NUTRITIONAL DEFICIENCY and MALNUTRITION can develop rather quickly, initiating a cascade of health consequences that can be difficult to reverse. It is important for caregivers and healthcare providers to monitor dietary intake and nutrition in the elderly, to make sure food and nutrient consumption is adequate. Basic NUTRITIONAL ASSESSMENT should be a component of most visits to the doctor and of every ROUTINE MEDICAL EXAMINATION.

Maintaining Healthy Nutrition Across the Age Spectrum

Healthy eating habits support the body in maintaining optimal health at any age. In combination with appropriate daily physical exercise, adequate nutrition often is the difference between full recovery and prolonged or incomplete recovery from health conditions that arise. These lifestyle factors also lower the risk for numerous health conditions.

See also CARDIOVASCULAR DISEASE PREVENTION; DIET AND HEALTH; LIFESTYLE AND HEALTH; NUTRIENTS; OBESITY AND HEALTH; PREVENTIVE HEALTH CARE AND IMMUNIZATIONS.

antioxidant A biochemical substance that attracts free radicals, unmatched molecules remaining as the waste byproducts of oxidation functions (energy conversion and release) within the body. Free radicals are associated with numerous health conditions, especially chronic diseases, though researchers do not yet fully understand their roles. Free radicals bind with other molecules, hijacking them from their intended destinations. The resulting rogue molecules do not have legitimate functions within the body and disrupt normal cellular functions. When an antioxidant molecule binds with a free radical, the resulting structure becomes a readily identifiable waste molecule that the body's natural processes then eliminate from the body.

Antioxidants are abundant in fruits and vegetables. The body also synthesizes some antioxidants such as COENZYME Q10. Carotenoids (components of vitamin A), vitamins C and E, the mineral selenium, and phytochemicals such as flavonoids and plant sterols are among the common dietary antioxidants. SOY, GREEN TEA, and GINKGO BILOBA are particularly high in such phytochemicals. Research suggests antioxidants play a vital role in stopping cancers before they gain any momentum as well as in slowing the progression and damage of chronic conditions such as ATHEROSCLEROSIS and DIABETES.

Though many NUTRITIONAL SUPPLEMENTS contain antioxidants, food-based antioxidants appear to have more potent effects through their numerous though little-understood interactions with one another. One exception is coenzyme Q10, which does not come from dietary sources but rather through processes within the body. Coenzyme Q10 supplements boost coenzyme Q10 levels in the body to have apparently the same effects as endogenous coenzyme Q10. Minerals such as copper and zinc help the body use antioxidants more effectively.

See also NUTRITIONAL THERAPY; PHYTOESTROGENS; SUN'S SOUP; VITAMIN AND MINERAL THERAPY.

appetite The sensation of feeling the desire to eat. Appetite represents complex hormonal, neurologic, and environmental interactions that correlate in varying proportions both to HUNGER, the body's physiologic signal that it needs food, and to learned behaviors for eating. Seeing, smelling, and thinking about food often trigger appetite. Many people also feel the desire to eat at conventional meal times, regardless of whether their bodies actually need food. Emotional circumstances may trigger appetite as well, particularly when there is an emotional or habitual connection between eating and feeling comforted.

The Mechanisms of Appetite

Three regions of the BRAIN work in collaboration and counterbalance to regulate appetite: the appetite center, the SATIETY center, and the hunger center. The appetite center resides within the brainstem, the most rudimentary structure of the brain that regulates functions necessary for survival. It responds to external sensory NERVE signals from the body that travel to the brain via the CRANIAL NERVES as well as to nerve signals that come from the cerebral cortex. Because signals from the cerebral cortex arise from activities of cognitive function (such as thought, memory, and emotion), their influence on the appetite center is within conscious control.

The hunger center resides within the HYPOTHALAMUS, a structure of the midbrain that integrates neurologic and hormonal activity to maintain essential body functions. The hunger center responds primarily to the level of GLUCOSE (the form of sugar that is the primary fuel for the body's cells) in the BLOOD, activating the appetite center when the blood glucose level drops. The hunger center's activation triggers a cascade of response from the hypothalamus that includes sending nerve signals to the appetite center and the cerebral cortex to stimulate the desire to eat, hormonal signals to the gastrointestinal tract to begin releasing DIGESTIVE HORMONES (such as gastrin, secretin, cholecystokinin, and pepsin), and neurohormonal signals that result in an increase of acetylcholine, a NEUROTRANSMITTER that facilitates smooth MUSCLE contraction, in the gastrointestinal tract. These events establish a cycle that continues until blood glucose levels rise. Because the hunger center responds to neurohormonal signals related to basic survival, neither it nor its influence on the appetite center is within conscious control.

The satiety center also resides in the hypothalamus near the hunger center. It responds to nerve signals from the hunger center and from the appetite center. As food enters the SMALL INTESTINE for the main phase of digestion, the small intestine releases peptide YY, a HORMONE that signals the satiety center. The satiety center in turn sends nerve messages to the hunger center and to the appetite center, signaling that the body no longer needs to consume food. Concurrently the balance of digestive hormones begins to shift, further signaling the satiety center as well as slowing the signals going to the appetite center.

Appetite Response

Appetite is a powerful mechanism intended to bring food (energy) into the body. Though aspects of appetite represent areas of conscious control, appetite response is not simply an issue of willpower or of survival. Some people eat a small amount, feel satisfied, and stop eating. Other people eat large amounts of food and do not feel satisfied, even when they begin to feel physically uncomfortable because they have eaten more than enough to fill their gastrointestinal tracts. Appetite appears to be a short-term feature of energy management designed to meet the body's daily energy needs; how appetite correlates with the body's available stores of surplus energy (in the form of body fat) remains a mystery.

There is some evidence that continued exposure to the smells of food without eating may signal both the satiety center and the appetite center that the body is consuming enough food, even when a person is only smelling, not eating, food. However, manipulating the appetite is not so easy. Establishing EATING HABITS that provide adequate CALORIE and nutrition intake helps maintain balance among the appetite, hunger, and satiety centers. This is particularly important for WEIGHT LOSS AND WEIGHT MANAGEMENT as well as for overall health maintenance.

See also DIGESTIVE ENZYMES; METABOLISM; OBESITY AND HEALTH; STARVATION.

beriberi A health condition resulting from long-term deficiency of thiamine (vitamin B_1). Beriberi affects neurologic, musculoskeletal, cardiovascular, and gastrointestinal structures and functions. Though common in developing parts of the world, beriberi occurs primarily in people who have gastrointestinal disorders that interfere with thiamine absorption and in long-term, chronic ALCOHOLISM. A BREASTFEEDING infant whose mother is thiamine deficient may also develop beriberi. Beriberi is also common among people whose primary food is white rice. Thiamine is necessary for cells in the body to convert GLUCOSE to energy and to convert glucose to energy storage forms (fat).

There are two main forms of beriberi: dry and wet. Dry beriberi is more common and affects primarily the NERVOUS SYSTEM and the musculoskeletal system. Wet beriberi affects primarily the cardiovascular system; its most apparent symptom is edema (swelling due to fluid accumulation), which accounts for the "wet" designation. People who have mild to moderate beriberi typically have distinctly one form or the other; people who have moderate to severe disease generally have both forms as the deficiency is severe enough to affect all body functions.

Symptoms and Diagnostic Path

The early symptoms of beriberi are the same for either the wet or the dry form and include

- fatigue
- difficulty concentrating and cognitive dysfunction
- irritability
- loss of APPETITE
- NAUSEA, VOMITING, and CONSTIPATION
- abdominal tenderness

As the condition progresses symptoms become specific for the body system affected. Neurologic and musculoskeletal (dry beriberi) symptoms include

- peripheral NEURITIS (INFLAMMATION of the nerves) or peripheral NEUROPATHY
- PARESTHESIA (disturbances of sensation such as tingling and numbness)
- cramps in the lower legs
- PAIN and weakness in muscles throughout the body
- difficulty walking and rising from a sitting or squatting position

Cardiovascular (wet beriberi) symptoms are those of congestive HEART FAILURE and include

- tachycardia (rapid HEART RATE)
- diaphoresis ("cold sweats")
- edema
- shortness of breath (DYSPNEA)

The diagnostic path begins with a careful assessment of the PERSONAL HEALTH HISTORY with an emphasis on EATING HABITS. BLOOD tests can measure the amount of thiamine in the blood as well as enzyme levels related to thiamine activity in the body. When symptoms are cardiovascular, the doctor is likely to conduct an ELECTROCARDIOGRAM (ECG) and an ECHOCARDIOGRAM.

Treatment Options and Outlook

Treatment is injections of thiamine until blood levels return to normal and symptoms begin to

subside. Cardiovascular symptoms generally improve within 24 hours, though underlying damage to the HEART may be permanent and require subsequent treatment. Neurologic and musculoskeletal symptoms may take several months to completely resolve. Dry beriberi generally resolves without residual complications except in the most severe cases, in which there may be permanent peripheral neuropathy (damage to the PERIPHERAL NERVES). Untreated beriberi is fatal, usually a result of cardiovascular collapse.

Maintenance therapy with vitamin B supplementation helps prevent RECURRENCE, especially in people who are not likely to receive adequate B vitamins from dietary sources. Most people who have thiamine deficiency are also deficient in other B vitamins and should take a vitamin B complex supplement product. People who have gastrointestinal disorders that interfere with their ability to absorb thiamine, such as PEPTIC ULCER DISEASE, may require ongoing thiamine injections.

Risk Factors and Preventive Measures

The sole risk factor for beriberi is inadequate consumption of dietary thiamine. Accordingly, maintaining adequate dietary consumption of foods that contain B vitamins prevents beriberi in most people. Food sources of thiamine include lean meats (notably pork), legumes, watermelon, acorn squash, and whole grains and whole grain products. Grain products such as breads and cereals produced in the United States are fortified with B vitamins, including thiamine. Highly refined and processed foods, especially white rice and white bread, contain minimal amounts of B vitamins, including thiamine, unless they are fortified. B complex vitamin supplements help ensure adequate intake. B vitamins are water-soluble so there is no risk for OVERDOSE.

See also ANEMIA; MALNUTRITION; NUTRITIONAL DEFICIENCY; NUTRITIONAL NEEDS; PELLAGRA; RICKETS; SCURVY; VITAMINS AND HEALTH.

calorie A unit of measure that denotes heat consumption. In nutrition and exercise, calories represent a measure of energy exchange. The calories in foods represent energy the body takes in, and the calories assigned to physical exertion represent energy the body expends. Recommended daily calorie intake guidelines represent the amount of energy a typical adult requires to carry out the activities of normal living. Taking in more calories than one expends results in weight gain (the body stores extra calories as fat), and expending more calories than one consumes results in weight loss (the body draws from stored energy to meet its needs). The steady state of weight maintenance occurs when there is a relative balance between the calories that enter the body and the calories the body uses.

See also METABOLIC EQUIVALENT (MET); NUTRIENTS; NUTRITIONAL NEEDS.

carbohydrate intolerance An enzyme deficiency that results in the body's inability to metabolize one or more forms of carbohydrate. The most common form of carbohydrate intolerance is LACTOSE INTOLERANCE, which affects up to 50 million Americans and results from a deficiency of the enzyme lactase. Other forms of carbohydrate intolerance are much less common though may result from deficiencies of maltase (necessary to metabolize maltose) and sucrase (also called isomaltase, necessary to metabolize sucrose).

The enzyme deficiencies responsible for carbohydrate intolerance may be congenital (absent from birth), acquired through a natural decline in DIGESTIVE ENZYMES through aging, or as a consequence of gastrointestinal disorders such as CELIAC DISEASE. RADIATION THERAPY and CHEMOTHERAPY treatments for cancer also can affect the cells that produce the various enzymes, resulting in enzyme depletion and intolerance of the corresponding carbohydrate.

The symptoms of carbohydrate intolerance often include abdominal cramping, flatulence (gas), and DIARRHEA. Children may fail to gain weight or grow appropriately. The diagnostic path may include an oral carbohydrate challenge, in which the person drinks a solution containing the suspect carbohydrate. BLOOD samples taken at certain intervals measure the amount of the sugar form present in the blood circulation. Because lactose intolerance results IN excessive hydrogen gas production, breath tests to measure hydrogen concentrations in the lungs are often diagnostic for lactose intolerance.

Many people can tolerate small amounts of substances that contain the sugars for which they are lacking enzymes. Avoiding larger amounts keeps symptoms in check. It is important for people who have carbohydrate intolerance to make sure they receive adequate intake of other NUTRIENTS in foods for which they have intolerance or to take supplements that supply them.

See also AGING, NUTRITION AND DIETARY CHANGES THAT OCCUR WITH.

cholesterol, dietary A sterol substance found in animal-based foods such as meats and dairy products. Dietary cholesterol under scrutiny in the 1970s when research connected high BLOOD cholesterol levels with increased risk for CARDIOVASCULAR DISEASE (CVD), notably ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). However, subsequent research has determined the true culprit is endogenous cholesterol—the cholesterol the LIVER synthesizes from the components of dietary saturated fats and trans fats. The liver makes about 80 percent of the cholesterol in the blood circulation, and it continues to make cholesterol as long as it receives the source materials (dietary fats) to do so. Dietary cholesterol has almost no role in this process.

Furthermore, researchers recognized it is not the cholesterol itself that is the problem. Cholesterol, which is important to health because it is essential for cell membrane repair and HORMONE production, has the consistency of a waxy liquid and does not dissolve in water or blood. Carrier proteins called lipoproteins, which the liver also produces, bind with cholesterol molecules so they can travel through the bloodstream. The more cholesterol molecules in the blood circulation, the more lipoproteins required to transport them through the blood. When there are high levels of lipoproteins in the blood some tend to "fall out" against the sides of the arteries, eventually forming plaques (hardened patches) that narrow and stiffen the arteries. These plaques are the early stages of ATHEROSCLEROSIS, the foundation of CAD.

There is very little correlation between the cholesterol in foods and the cholesterol in the blood circulation. Rather, the amounts of saturated fats and trans fats in the diet determine blood levels of cholesterol in most people. Cholesterol and saturated fats co-exist in many animal-based foods, however, so a diet heavy in these foods contributes to higher-than-healthy cholesterol and lipoprotein levels in the blood. Health experts recommend limiting dietary cholesterol to 200 milligrams a day for people who have no increased risk for CVD. Doctors may recommend a lower limit for people who have, or have increased risk for, CVD.

See also CARDIOVASCULAR DISEASE PREVENTION; CHOLESTEROL BLOOD LEVELS; DIET AND HEALTH; HYPERLIPIDEMIA; LIFESTYLE AND HEALTH; NUTRIENTS; TRIGLYCERIDE BLOOD LEVEL; TRIGLYCERIDES, DIETARY.

D–H

diet and health The effects foods and EATING HABITS have on health and HEALTH RISK FACTORS. As diet is the primary means by which the external environment enters the internal environment of the body, much research focuses on how diet affects health in general as well as the risk for numerous health conditions. The obvious correlations are those between specific nutrient deficiencies, conditions such as BERIBERI and SCURVY. Other health conditions that have major dietary connections are the diseases that claim the most lives and cause the most disability among Americans: cancer, CARDIOVASCULAR DISEASE (CVD), DIABETES, OBESITY, and OSTEOPOROSIS. Diet—what foods and how much of them a person eats—has emerged as a significant risk factor for these conditions.

On the whole, the body has a remarkable ability to use the substances it receives through diet to conduct the functions of living. This ability in part stems from the processes of METABOLISM that reduce all NUTRIENTS to their absolute basic components, amino acids and sugars that eventually become GLUCOSE. The body's numerous systems then reassemble those components into the substances they require. In large part the body can subsist in reasonable health on a marginal diet. Eventually, however, the shortcomings become problematic and begin contributing to health conditions. For example, a diet low in fruits, vegetables, and whole grains lacks a consistent supply of the vitamins and minerals the body needs to manage its energy needs, maintain immune functions, and regulate body activities. The consequences of inefficient metabolism range from molecular, which may include the accumulation of free radicals or disruptions in protein sequencing of GENETIC CODE, to overt disease such as CVD.

Correlations between diet and disease are sometimes difficult for researchers to quantify. For example, people who eat a diet high in meats and saturated fats have a higher incidence of COLON cancer than people who eat a diet that is primarily vegetarian and low in fat. The reasons for this are imprecise, however, and likely represent an integration of factors of which diet is only one consideration. Other correlations are more precise, such as those that link high dietary saturated fat, high CHOLESTEROL BLOOD LEVELS, and ATHEROSCLEROSIS. Foods also appear to influence mood and behavior, though again the precise mechanisms of these interactions remain unknown.

Diet can bolster health as well. Supplying the body with the nutrients it needs allows it to function with optimal efficiency. In such a state the body's own systems are fully active to resist damage and respond promptly when injury or illness occurs. Health experts believe lifestyle factors such as diet and exercise have the ability to eliminate as much as 85 percent of HEART disease, obesity, and type 2 DIABETES, and reduce the risk for COLORECTAL CANCER, STOMACH CANCER, and possibly BREAST CANCER and PROSTATE CANCER.

See also ANTIOXIDANT; CANCER PREVENTION; CARDIOVASCULAR DISEASE PREVENTION; DIABETES PREVENTION; FOOD SAFETY; HEALTHY PEOPLE 2010; LIFESTYLE AND HEALTH; OBESITY AND HEALTH.

enteral nutrition Nutritional supplementation or replacement when a person cannot acquire the necessary NUTRIENTS by eating, typically administered via a nasogastric tube or surgically inserted tube, commonly called a feeding tube. Long-term enteral nutrition may become a QUALITY OF LIFE issue or an end-of-life concern, especially for those who become unable to make and express

their desires. An advance directive allows a person to establish in writing his or her desires about such matters, mitigating family conflict about making the decision on behalf of the person.

Types of Feeding Tubes for Enteral Nutrition

A nasogastric tube is a thin, flexible catheter the doctor inserts through the NOSE, down the back of the THROAT, through the ESOPHAGUS, and into the STOMACH. The insertion process is somewhat uncomfortable but does not require anesthetic, though the doctor generally sprays a topical anesthetic on the back of the throat to numb the gag REFLEX. A nasogastric tube is for short-term use, usually no longer than a few weeks. The nasogastric tube blocks the nostril through which it enters, and becomes irritating to the nasal mucosa as well as the SKIN around the nostril.

Surgically inserted tubes are for long-term use and are generally somewhat sturdier though still narrow and flexible. They enter the stomach or SMALL INTESTINE through an opening in the abdominal wall. The most common type is the percutaneous endoscopic gastrostomy (PEG) tube, also called a gastrostomy tube or G tube, for long-term use. With the person under general ANESTHESIA, the doctor makes a small incision through the abdominal wall for the insertion of the tube. An endoscope passed into the stomach via the throat and esophagus guides the doctor in placing the tube. A small balloon at the tip of the tube, inflated with saline solution, lodges the tube in the stomach. The surgical wound, called a stoma, heals in 7 to 10 days.

A gastric button is an alternative to a PEG tube. After the stoma is completely healed, the person can remove the tube and replace it with a gastric button, a pluglike device that fits into the stoma to block the opening. At feeding times the person (or caregiver) removes the button, reinserts the tube, and administers the enteral nutrition solution. Some people find a gastric button more discreet and less intrusive. A third surgical alternative is a tube placed into the JEJUNUM, the middle segment of the small intestine. A jejunostomy tube, or J tube, may be necessary for a person who has had a GASTRECTOMY (surgical removal of the stomach) such as to treat STOMACH CANCER, or has severe GASTROESOPHAGEAL REFLUX DISORDER (GERD) that negates a PEG or other gastric tube. Because the small intestine accepts limited volume, enteral nutrition via J tube is a continuous infusion.

Conscientious PERSONAL HYGIENE is essential with either kind of tube to prevent skin irritation (around the nostrils with a nasogastric tube and at the stoma site with a surgically placed tube) and INFECTION (more of a concern with a surgically placed tubes).

Enteral Nutrition Feeding

Enteral feeding may be continuous or intermittent, depending on the person's health status and NUTRITIONAL NEEDS. Enteral nutrition administered via surgically inserted tubes can provide adequate sustenance for years. Commercially prepared enteral nutrition solutions, most of which require a doctor's prescription, are of appropriate viscosity to avoid clogging the tube. They have high nutritional density and are available in various formulations to meet individual nutritional needs. The formula and the person's requirements determine the frequency and rate of infusions.

In some situations doctors may recommend enteral nutrition formulas that are palatable enough to take by MOUTH, typically in situations in which a person has difficulty chewing or swallowing and does not want a feeding tube, or who generally gets adequate nutrition from eating but would benefit from the nutritional boost of an enteral nutrition formula. Some products are available over the counter (OTC) without a doctor's prescription. Because excesses of some nutrients can cause health problems or interfere with prescribed medications, people who are considering such OTC products should discuss the approach with their doctors first.

See also ENDOSCOPY; NUTRITIONAL ASSESSMENT; PARENTAL NUTRITION.

feeding tube See ENTERAL NUTRITION.

food–drug interactions See DRUG INTERACTION.

hunger The body's physiologic indication that it needs energy (food). Hunger occurs when the STOMACH and SMALL INTESTINE are empty and manifests as physical sensations of discomfort and even PAIN that result from contractions of the stomach.

Hunger sends HORMONE and NERVE signals to the APPETITE and hunger centers in the BRAIN, each of which responds with other neurohormonal messages that intensify the physical and psychological urges to eat. Hunger subsides only when the body receives food (in contrast to appetite, which abates after time even when the person does not eat).

See also DIGESTIVE ENZYMES; DIGESTIVE HORMONES; METABOLISM; STARVATION.

hydration Maintenance of the body's fluid level. About 60 percent of the body's weight is water. The typical adult requires three quarts (two liters) of water daily to remain adequately hydrated. Health experts recommend drinking six to eight cups of water each day to meet this need, though most people acquire much of the water they need through the foods they eat. Many foods, notably fruits and vegetables, have high water content that helps supply the body with water. Soups, sauces, fruit and vegetable juices, and pastas and rice cooked in water also supply fluid to the diet. Health experts consider water a vital nutrient because the body cannot live without it. Though water contains no calories, it does contain trace minerals that are necessary for metabolic functions. A person can survive only about five to seven days without water.

Thirst is not a good indication of proper hydration. By the time a person feels thirsty, the body is experiencing significant fluid depletion. In DEHYDRATION, many people do not feel thirsty.

DEHYDRATION is a serious condition that results from inadequate water consumption, and can occur much more rapidly than expected during intense physical exercise and in hot temperatures as the body loses significant water through sweat. Distance athletes and WEEKEND WARRIORS are at particular risk for dehydration during competition, the former because their efforts are so intense that it is difficult to drink enough water often enough to keep up with water loss and the latter because they often do not realize the intensity of their efforts and fail to properly hydrate before and during competitive activities including swimming and other water sports. Dehydration leads to electrolyte imbalances as the salts in the body become more concentrated, resulting in numerous physiologic consequences including mental confusion and impaired cognitive function, irregular HEART RATE, fluctuations in BLOOD PRESSURE, and MUSCLE cramps.

WATER CONSUMPTION FOR HYDRATION DURING PHYSICAL ACTIVITY

90 minutes before activity: 12 ounces of cold water
15 minutes before activity: 12 ounces of cold water
During activity: 4 ounces of cold water every 15 minutes
15 minutes after activity: 16 ounces of cold water

Fluids that contain sugar or CAFFEINE actually draw water from the body. Excess sugar pulls water into the gastrointestinal tract as it makes its way through the digestive process. Caffeine is a mild diuretic, acting on the KIDNEYS to cause them to extract more water from the BLOOD. Beverages such as sodas (soft drinks) also contain high quantities of electrolytes, which are minerals in the form of salts. These, too, may act on the kidneys to increase the water the kidneys pull from the blood to pass with the URINE.

In a clinical context hydration may refer to the long-term infusion of fluids via PARENTERAL NUTRITION or ENTERAL NUTRITION (feeding tube) into a person who is in a PERSISTENT VEGETATIVE STATE as a means of preserving life.

See also COGNITIVE FUNCTION AND DYSFUNCTION; CONDITIONING; END OF LIFE CONCERNS; HEAT EXHAUSTION; HEAT STROKE.

L–M

lactose intolerance The inability to digest lactose, a disaccharide sugar in milk and other dairy products. Lactose intolerance occurs because of a deficiency of the enzyme lactase, which is necessary to break down lactose into simpler sugar molecules. It is the most common form of CARBOHYDRATE INTOLERANCE, affecting an estimated 50 million Americans. Lactose intolerance may be congenital (present at birth), occur as a consequence of a disease process that affects the cells that produce lactase (such as CELIAC DISEASE), or develop with aging as the number of lactase-producing cells naturally declines.

Congenital lactose intolerance becomes apparent when a young child begins drinking cow's milk, which is high in lactose. The doctor can usually confirm the diagnosis with a lactose challenge test in which the child drinks a solution that contains lactose. Breath samples taken at certain intervals allow measurement of hydrogen, which increases when lactose remains undigested in the gastrointestinal tract.

Switching to a fortified SOY formula nearly always eliminates symptoms when the child is young. As the child grows older, trial and error will tell whether he or she can eat small amounts of other dairy products such as cheese and ice cream. Many people who have lactose intolerance produce enough lactase to digest small amounts of lactose. Lactase enzymes are available without a doctor's prescription; added to milk, they act on the lactose to split it into its composite sugars. Within 24 hours the milk will be 70 to 90 percent lactose-free. This approach allows the child to benefit from the numerous NUTRIENTS milk and dairy products provide. Lactose intolerance generally does not affect an individual's overall general health, as long as the person acquires necessary nutrients through alternative foods or via supplements.

See also AGING, NUTRITION AND DIETARY CHANGES THAT OCCUR WITH.

malnutrition A state of multiple nutrient depletion that alters body functions. Infants, the elderly, and people who have active cancer, ALCOHOLISM, OBESITY, or chronic health conditions are most susceptible to malnutrition. Malnutrition may develop when a person does not eat enough food, eats a very narrow selection of foods, or eats too much food. Malnutrition is possible with extended adherence to fad diets that limit food types and when the diet primarily contains foods that have low NUTRIENT DENSITY such as "junk" foods. The most severe presentations of malnutrition are the polar extremes of STARVATION and obesity.

In the United States malnutrition resulting from inadequate food or nutrient consumption occurs most often in the chronically ill, the very young, and the very old. Most people who have significant obesity have some degree of nutrient imbalance, not only among the energy NUTRIENTS but also of vitamins, minerals, and other micronutrients. People who have alcoholism, serious chronic health conditions such as HIV/AIDS, or gastrointestinal MALABSORPTION disorders including INFLAMMATORY BOWEL DISEASE (IBD) and CELIAC DISEASE or are also vulnerable to malnutrition.

Symptoms and Diagnostic Path

Early malnutrition can be difficult to detect though initial indications may include dry SKIN, pallor, swollen or bleeding gums, PETECHIAE (pinpoint hemorrhages under the skin), MUSCLE weakness and atrophy, and disturbances of sensory perception (PARESTHESIA) in both inadequate and

excessive nutrient consumption. The diagnostic path includes a comprehensive medical examination, height and weight measurements, careful assessment of EATING HABITS, body composition assessment, and a complete BLOOD count (CBC) as well as other blood tests to measure nutrient levels. A BODY MASS INDEX (BMI) below 17 kilograms per meter squared (kg/m^2) is generally diagnostic of inadequate consumption; a BMI greater than 30 kg/m^2 is generally diagnostic of obesity.

Treatment Options and Outlook

Treatment for malnutrition focuses on correcting the nutritional deficiencies that exist, which usually means generalized nutritional supplementation until symptoms resolve, along with dietary changes to improve overall nutrition. People who have obesity often have significant nutritional deficiencies even though their food consumption may be excessive. The US Department of Agriculture (USDA) publishes a food pyramid with recommendations for food consumption to meet NUTRITIONAL NEEDS. Daily physical activity, such as walking, improves the body's ability to digest, absorb, and metabolize nutrients and also is key to weight management.

The success of treatment depends on the severity of the malnutrition at the time of diagnosis, the status of underlying or contributing causes (such as gastrointestinal or metabolic disorders), the person's age, the availability of nutritious foods, and the ability to feed oneself. Many of the symptoms of malnutrition resolve without residual complications, though severe symptoms may result in permanent damage.

Risk Factors and Preventive Measures

The most significant risks for malnutrition are inadequate food consumption and malabsorption disorders that keep the body from extracting needed nutrients during digestion. Those who cannot easily feed themselves are most susceptible to inadequate consumption. People who diet frequently or follow restrictive eating habits (such as those who follow a vegan diet) are at risk for deficiency in key nutrients normally in the foods they are not eating. APPETITE loss contributes to decreased food consumption in serious chronic conditions such as HIV/AIDS and CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). Untreated disorders of specific NUTRIENT DEFICIENCY such as BERIBERI and SCURVY lead to generalized malnutrition.

It is important to eat or provide a variety of foods in the appropriate quantities, as the USDA food pyramid recommends, especially for young children and the very elderly, for whom caregivers sometimes assume intake is nutritionally adequate. Though most healthy children and adults who can feed themselves can acquire the nutrients they need through diet, nutritional supplements can provide a steady and certain source of necessary nutrients for people who have chronic health conditions or who do not eat adequately.

See also AGING, NUTRITION AND DIETARY CHANGES THAT OCCUR WITH; ANEMIA; MINERALS AND HEALTH; OBESITY AND HEALTH; OSTEOPOROSIS; PELLAGRA; VITAMIN AND MINERAL THERAPY; VITAMINS AND HEALTH.

minerals and health Minerals are inorganic micronutrients essential for health and the body's proper development and function. Minerals are abundant in nature and in most foods, and facilitate numerous actions in the body. Six major minerals (also called macrominerals) and nine trace minerals (also called microminerals) are essential for health and the body's proper growth and development; the body cannot survive without them. Numerous other trace minerals are present in the body and presumably important for the body's functions but researchers do not understand their roles. Minerals within the body are also called electrolytes or ions because they are polarized (carry a positive or negative charge).

Major Minerals

The body requires substantial amounts of the major minerals, which are essential for the daily activities that keep the body alive and functional. The body of a person who weighs 160 pounds contains 3 pounds of calcium, 1½ pounds of phosphate, ½ pound of potassium, ¼ pound each of sodium and chloride, and a little over 1 ounce of magnesium.

The major minerals work closely with each other and with the vitamins. For example, calcium, phosphate, and magnesium are essential for BONE mineralization though their passage into the bone requires the presence of vitamin D in the

BLOOD circulation. As well, 85 percent of the body's phosphate is bound to calcium, most of it in the bones. Sodium, chloride, and potassium regulate the contraction of MUSCLE cells (including those in the HEART) and the balance of fluid in the body.

Deficiencies of the major minerals can significantly affect the functioning of the heart, KIDNEYS, neurologic system, bones, and muscles. The most common deficiencies of the major minerals are of calcium, which can result in OSTEOPOROSIS and heart ARRHYTHMIA, and potassium, which occurs most commonly in people who take diuretic medications to treat conditions such as congestive HEART FAILURE and kidney disease.

Mineral toxicities of the major minerals are uncommon though can occur in people who take diuretic medications (when the kidneys keep more of the mineral in the blood circulation, allowing its level to accumulate) and in circumstances of OVERDOSE such as from taking excessive mineral supplements. Overdose of magnesium can disrupt the functions of the neurologic and cardiovascular systems severely enough to be fatal. Some people develop HYPERTENSION (high BLOOD PRESSURE) with long-term dietary excesses of sodium and chloride, though most doctors do not consider this toxicity.

Calcium The hormones PARATHYROID HORMONE and calcitonin, along with the HORMONE form of vitamin D, calcitriol, regulate the amounts of calcium in the blood. Calcium is essential for bone STRENGTH and BONE DENSITY. It is also a key ion (electronically charged particle) with roles in NERVE signals and muscle contraction. Calcium channel blockers are drugs that regulate HEART RATE and function by blocking the passage of calcium ions in the heart muscle (MYOCARDIUM).

Sodium and chloride Sodium and chloride are present in chemical combination with each other. Sodium is a positively charged ion that is abundant in the fluid outside the cells (extracellular fluid) and regulates fluid balance in the body. Chloride is a negatively charged ion that occurs primarily in equilibrium with sodium in the extracellular fluid, assisting with fluid balance. Special molecular sensors in the glomeruli of the kidneys continually monitor the levels of sodium and chloride in the blood circulation, which determines how much of these minerals the kidneys will reabsorb which in turn determines how much water the kidneys hold for circulation in the blood. Diuretic medications act on the molecular sensors in the glomeruli to limit their ability to reabsorb these minerals.

TABLE SALT

Table salt is sodium chloride, about 40 percent sodium and 60 percent chloride. One teaspoon of table salt contains two grams of sodium and three grams of chloride.

Potassium Potassium is a positively charged ion that is abundant in the fluid within the cells (intracellular fluid). It is a key player in fluid balance within the body, and also in the transmission of nerve impulses across neurons. The kidneys also regulate the amount of potassium in the blood circulation. Long-term diuretic therapy can deplete potassium because potassium passes from the blood along with sodium and chloride though its levels in the circulation are much lower. Chronic VOMITING and DIARRHEA also result in losses of potassium. Chronically low potassium levels cause hypertension, though researchers do not understand the mechanisms of this.

Phosphate This mineral is integral to nucleic acid formation (DNA and RNA) and cell reproduction. It also is a component of numerous enzymes, is necessary for activation of the B vitamins, and participates in energy conversion. Various forms of phosphate bind with lipids to form the primary structure of the cell membrane for every nucleated cell in the body.

Magnesium Magnesium is essential for cellular METABOLISM and energy conversion, influencing the efficiency with which cells use GLUCOSE and serving as a component of numerous enzymes. Magnesium is also essential for initiating the contraction of muscle cells, facilitating nerve signals, integrating certain IMMUNE SYSTEM functions, and regulating blood pressure.

Trace Minerals

Trace minerals are present in the body in barely measurable amounts, though their absence can have far-reaching consequences for overall health. Zinc and copper are essential for HEALING and the

ESSENTIAL MINERALS

Mineral	Dietary Sources
Major Minerals (Macrominerals)	
calcium	dairy products fortified orange juice and SOY milk spinach, broccoli, green beans legumes, nuts, tofu canned sardines, salmon, herring (with bones) molasses sweet potatoes (with skin) oranges, raisins, watermelon
chloride	table salt processed foods (as a preservative) pork, ham, beef, chicken, turkey, fish
magnesium	all foods highest in meats, poultry, fish, legumes
phosphate	all foods
potassium	all foods
sodium	table salt processed foods (as a preservative) pork, ham, beef, chicken, turkey, fish
Trace Minerals (Microminerals)	
chromium	pork, ham, beef, chicken, turkey, fish, shrimp raw fruits, vegetables, whole grains
copper	whole grains and whole grain products finfish, shellfish, crab, lobster legumes, tofu nuts, seeds
fluorine	fluoridated drinking water salt water seafood (finfish, shellfish, crab, lobster, kelp)
iodine	iodized table salt salt water seafood (finfish, shellfish, crab, lobster, kelp)
iron	canned clams fortified breads and cereals whole grains spinach, broccoli, peas, green beans, potatoes (with skin), artichokes parsley legumes, tofu

Mineral	Dietary Sources
Trace Minerals (Microminerals)	
iron (continued)	pork, ham, beef, chicken, turkey, fish, shrimp raisins
manganese	whole grains and whole grain products legumes, nuts, seeds finfish, shellfish, crab, lobster
molybdenum	legumes, nuts, seeds liver whole grains and whole grain products fortified breads and cereals
selenium	whole grains and vegetables grown in selenium-rich soil salt water finfish, shellfish, crab, lobster pork, ham, beef, lamb from animals who graze on selenium-rich land
zinc	oysters, clams, crab, shrimp, lobster legumes, nuts, seeds, tofu dairy products, especially cheeses peas, spinach, broccoli, corn, potatoes (with skin)

formation of new tissues (including growth) and are crucial for oxidative reactions in the cells. The body requires iron to synthesize HEMOGLOBIN, the protein that transports oxygen through the blood circulation. Fluorine strengthens TEETH and bones and increases the resistance of the teeth to bacterial invasion resulting in DENTAL CARIES (cavities). The THYROID GLAND requires iodine to synthesize thyroid hormones, which regulate metabolism. Selenium is a potent ANTIOXIDANT that may be a key player in CANCER PREVENTION. Manganese and molybdenum are essential cofactors for numerous enzymes vital to metabolic functions. Chromium aids metabolism of carbohydrates and fats.

Deficiencies or toxicities of some trace minerals can have significant and potentially fatal consequences for health. Iron deficiency causes ANEMIA, reducing the amount of oxygen that reaches the tissues through the blood circulation. Excessive iron accumulates in organs such as the heart and LIVER, such as occurs with HEMOCHROMATOSIS, eventually causing failure of those organs. Acute iron overdose is often fatal.

WILSON'S DISEASE is a genetic disorder in which the body cannot metabolize copper, allowing copper to accumulate in the heart, liver, PANCREAS, and BRAIN. Unchecked, this accumulation is fatal; treatment is curtailed intake of foods containing copper. High intake of zinc blocks copper metabolism, which is therapeutic in Wilson's disease but hazardous otherwise. Iodine deficiency causes HYPOTHYROIDISM, and iodine excess causes GOITER. Untreated hypothyroidism in a pregnant woman or an infant causes irreversible brain damage. In the United States table salt includes iodine to help ensure adequate iodine intake.

See also CELL STRUCTURE AND FUNCTION; HEALTHY PEOPLE 2010; NUTRITIONAL NEEDS; NUTRITIONAL SUPPLEMENTS; NUTRITIONAL THERAPY; POISON PREVENTION; VITAMINS AND HEALTH.

N

nutrient density The nutritional value of a particular food, generally presented as an assessment of the quantity and quality of NUTRIENTS the food delivers per CALORIE. Foods that contain multiple minerals and vitamins per calorie have high nutrient density; those that do not have low nutrient density. Generally the less processed a food is, the higher its nutrient density. Fruits, vegetables, legumes, seeds, whole grains, and nuts have high nutrient density. Prepared dinners, cookies, crackers, chips, candy, and other such food products have comparatively low nutrient density. Some prepared foods, such as cakes and pastries, have relatively little nutritional value beyond the energy forms (carbohydrate and fat) they deliver. Though many prepared foods are not devoid of nutrients, they deliver significantly more calories for comparable nutrient levels. Foods with higher nutrient density also tend to be more filling.

See also EATING HABITS; METABOLISM; NUTRITIONAL NEEDS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

nutrients Substances that participate in METABOLISM. Macronutrients deliver energy. The three macronutrient groups are carbohydrate, fat, and protein. Micronutrients facilitate the biochemical actions that convert macronutrients into energy. The main groups of micronutrients are vitamins and minerals. Supportive nutrients include phytochemicals (plant-based biochemicals such as flavonoids and plant sterols) and the numerous trace minerals and other chemicals that are present in the body and have roles in metabolism, though researchers do not fully understand those roles. The final nutrient is water. Essential nutrients are those the body must acquire from sources outside itself, such as foods. Other nutrients, though no less important to health, are nonessential because the body can synthesize them from substances within it.

Macronutrients

The macronutrients—carbohydrates, fats, and proteins—are the body's energy sources. The amounts and ratios of them that an individual needs vary according to age, gender, activity level, and health status. Metabolism reduces all macronutrients ultimately to GLUCOSE. The body stores any excesses (amounts the body does not immediately use for energy) as glycogen and fat, regardless of the source macronutrient. Per gram carbohydrates and proteins yield four calories of energy; fats, which represent stored energy, yield nine calories per gram.

The body must use in some way all of the energy that enters it in the form of food, either through immediate consumption or storage. Glycogen, which the LIVER produces and stores, is an intermediate storage form that can supply about 12 hours of energy. The liver also produces fat, which adipose cells throughout the body store (body fat). The body in healthy balance warehouses enough body fat to supply energy for six to eight weeks.

In 2005 dietary recommendations shifted from a percentage allocation for macronutrient consumption to a stance of moderation in choice with a focus on managing overall CALORIE intake across the spectrum of energy nutrients. Health experts concur that people need a wide variety of nutrients and individual needs vary. Focusing on the quality of foods within each macronutrient group allows people to make choices that meet their personal needs and tastes, yet still meet the nutritional needs of their bodies in healthful ways.

Carbohydrates Carbohydrates are chemical structures consisting of oxygen, carbon, and

hydrogen. Nutritionists further classify carbohydrates as monosaccharides (single molecule), disaccharides (two molecules), and polysaccharides (multiple molecules). Monosaccharides and disaccharides are simple carbohydrates; polysaccharides are complex carbohydrates. Nearly all foods contain or deliver as a product of metabolism some form of carbohydrate. Monosaccharides and disaccharides convert to energy fairly quickly after consumption; the sugars from fruits and fruit juices and from candies and sodas (soft drinks) can enter the blood circulation within 10 minutes. Polysaccharides such as pastas take longer for the body to digest and metabolize, up to several hours.

Polysaccharides are starches and fibers. Starches are storage forms of glucose the LIVER converts to glycogen. Fibers are structural components of plants that the body cannot digest. Some forms of fiber, such as pectin, are soluble (dissolve in water). These fibers acquire a gel-like consistency in the intestines that bind with lipids (including cholesterol), BILE, and other substances. The primary dietary sources of soluble fibers are fruits, oats, and legumes. Nonsoluble fibers absorb water but do not change consistency. These fibers add bulk to digestive waste in the large intestine, aiding the COLON in moving the waste through and out of the body. Though not itself a nutrient, fiber is essential for the healthy function of the gastrointestinal tract.

CARBOHYDRATES

Monosaccharides		
GLUCOSE	fructose	galactose
Disaccharides		
lactose	maltose	sucrose
Polysaccharides		
cellulose	fiber	glycogen

Enzymes carry out the chemical actions that metabolize carbohydrates to the end form of glucose. Carbohydrate digestion begins in the MOUTH with the aid of amylase, an enzyme in the saliva. Amylase breaks down dietary carbohydrates into smaller polysaccharides and disaccharides. Because the STOMACH does not contain any enzymes that metabolize carbohydrates, the next stage of carbohydrate digestion takes place in the SMALL INTESTINE. The enzymes lactase, maltase, and sucrase break down lactose, maltose, and sucrose, respectively. Lactose and sucrose each produce one molecule of glucose; maltose produces two. From the small intestine the monosaccharides enter the BLOOD circulation. Fructose and galactose travel to the liver where chemical processes convert them to glucose. Depending on the body's needs, the liver may further convert glucose to glycogen for storage.

Fats (lipids) Dietary fats are chemical combinations of carbon and hydrogen atoms that form structures called fatty acids. The number of hydrogen atoms in a fatty acid determines whether the fat is saturated or unsaturated, which is one of the most important features of the fat from a health perspective. A fatty acid's saturation determines how the fat behaves in the body.

Saturated fats, which come primarily from animal-based foods such as meats and dairy, contribute to elevated CHOLESTEROL BLOOD LEVELS, a risk factor for CARDIOVASCULAR DISEASE (CVD). Saturated fats are the primary source material for the liver's production of cholesterol and the carriers that transport them through the blood, lipoproteins. Palm oil and coconut oil are also saturated fats. Saturated fats are solid at room temperature.

TRANSFORMED THINKING ABOUT TRANS FATS

In the 1980s and 1990s researchers and doctors believed trans fats, created through a manufacturing process called hydrogenation that adds hydrogen atoms to unsaturated fatty acid structures to make them more stable in food products, were less harmful for health than the saturated fats they were marketed to replace. However, further research demonstrated that trans fats are instead considerably more harmful to health, causing a rapid and significant rise in blood cholesterol levels and thus dramatically raising the risk for CARDIOVASCULAR DISEASE (CVD). Health experts now recommend avoiding trans fats; and in 2006, US regulations began requiring food labels to list trans fat content.

Unsaturated fats come from plant-based foods. Commonly called oils, unsaturated fats are liquid at room temperature. They are monounsaturated or polyunsaturated, depending on their chemical

configurations. Unsaturated fats, in moderation, appear to help lower blood cholesterol levels. Polyunsaturated fats include safflower, corn, and sunflower oils. Monounsaturated fats, which many health experts believe offer the greatest health benefits among the fatty acids, include olive, canola, and peanut oils as well as olives, avocados, almonds, pecans, cashews, and peanuts. Many "vegetable oil" products blend oils from different sources.

Trans fatty acids, or trans fats, are processed fats that contain extra hydrogen atoms to make them more solid at room temperature and more resistant to oxidative degradation than the base fatty acids are in their natural forms. Sometimes called hydrogenated fats, trans fats raise blood cholesterol levels higher and faster than do saturated fats. The most common dietary sources of trans fats are margarines, shortening, and partially hydrogenated cooking oils. Processed baked goods, snack foods, fried foods, and fast foods are common dietary sources of trans fats.

OMEGA-3 FATTY ACIDS AND HEALTH RISK REDUCTION

Research suggests that tipping the balance to favor consumption of omega-3 fatty acids can significantly lower the risk for HEART disease and cancer (especially PROSTATE CANCER and BREAST CANCER) in some people. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are two omega-3 fatty acids found in high concentrations in mackerel, salmon, lake trout, herring, sardines, and anchovies. The American Heart Association recommends two servings weekly of any of these fish.

The body requires fatty acids for numerous functions beyond energy, including HORMONE synthesis and cell membrane integrity. Nearly all fatty acids, in foods and in the body, take the form of triglycerides. The essential fatty acids are linoleic acid and linolenic acid, from which the body can synthesize other fatty acids. Linoleic acid is an omega-6 fatty acid; its primary dietary sources are meats, dairy products, and vegetable oils. Linolenic acid is an omega-3 fatty acid; soybeans, flaxseed and soybean oils, nuts, and seeds are its primary dietary sources. The body requires these fatty acids in relative balance. EATING HABITS that disproportionately deliver linoleic acid (saturated fats such as in meats) appear to correlate with increased risk for CVD (notably HYPERTENSION) and some types of cancer (notably hormone induced).

Proteins Dietary proteins, also called peptides, are chains of amino acids; amino acids are chemical structures (molecules) of carbon, hydrogen, oxygen, and nitrogen. Of the hundreds of amino acids in the body, 20 combine in various forms to create the majority of the body's proteins. Nine are essential, meaning they must enter the body from outside sources such as foods. Using these nine amino acids and other substances within the body, the body synthesizes all the other amino acids it needs and combines the amino acids to create proteins. Proteins are key messenger substances in the body. DNA (deoxyribonucleic acid), the GENETIC CODE each nucleated cell contains, is a protein strand. Other proteins carry its instructions to molecules throughout the body, giving the directions for the amino acid sequences that are the foundation of the body's structure and function.

Dietary proteins are also chains of amino acids and are complete or incomplete, according to whether the protein chain contains all nine essential amino acids (complete) or not (incomplete). Animal-based foods (meats, poultry, fish, and dairy) and soybeans provide complete dietary proteins. Plant-based foods provide incomplete proteins, though combining consumption of different plant-based foods can deliver a combination of proteins that are complete. Dietary variety is the most effective way to ensure the body receives adequate amounts of all the essential amino acids.

AMINO ACIDS

Essential Amino Acids		Nonessential Amino Acids	
histidine	isoleucine	alanine	argine
leucine	lysine	asparagine	aspartic acid
methionine	phenylalanine	cysteine	glutamic acid
threonine	tryptophan	glutamine	glycine
valine		proline	serine
		taurine	tyrosine

After consumption dietary proteins undergo digestion and metabolism, processes that break them down to their amino acid structures. The body then reassembles the amino acids into structures it requires for its functions. The body even-

tually metabolizes excess amino acids to glucose, glycogen, and fat. Though muscles in the body are primarily protein structures, eating large quantities of protein does not build MUSCLE mass; the body uses dietary protein only to supply the components it needs to craft its own proteins. Protein deficiency can be a health concern for vegans, who must take extra care to eat a wide variety of protein-rich plant-based foods to meet their protein needs.

Micronutrients

The key groups of micronutrients are vitamins and minerals, both of which facilitate the processes of energy conversion within the body and are essential for life. Vitamins are organic substances useful to the body only in their whole forms; cooking and processing easily destroy many vitamins. Vitamins are also the source of many antioxidants, biochemicals that remove free radicals (rogue molecules that are the waste byproducts of metabolism) from the body. Researchers believe the cumulative damage free radicals cause contributes to many health conditions, including CVD and cancer. Minerals are inorganic substances abundant in the environment that enter food sources directly (from the soil and water, as with plants) or indirectly (from the plants that animals eat). Minerals remain chemically unchanged from sources to their uses in the body, even when they bind with each other or with other substances.

Supportive Nutrients

Foods contain numerous substances that provide supportive action for nutrients. Key among them is the group called phytochemicals. Among the most prominent of these are the carotenoids, flavonoids, lignans, phenolic acids, phytosterols, PHYTOESTROGENS, and protease inhibitors. Though a number of phytochemicals have achieved recognition for their individual effects on health, the strongest health benefits appear to come from phytochemicals collectively. Health experts recommend going straight to the source for supportive nutrients, acquiring them through fresh fruits and vegetables, legumes, and whole grains.

Other supportive nutrients include minerals such as sulfur; amino acid derivatives such as carnitine and choline; and inositol, a substance the body synthesizes from glucose. Sulfur is present in many animal-based foods and occurs in the body as an ingredient of proteins, some B vitamins, and some hormones. Carnitine, choline, inositol, and numerous similar substances act somewhat like vitamins in the body, though the body synthesizes them.

See also AGING, NUTRITION AND DIETARY CHANGES THAT OCCUR WITH; ANTIOXIDANT; BODY FAT PERCENTAGE; CARBOHYDRATE LOADING; CELL STRUCTURE AND FUNCTION; DIET AND HEALTH; MINERALS AND HEALTH; PHENYLKETONURIA (PKU); STARVATION; TRIGLYCERIDE BLOOD LEVEL; TRIGLYCERIDES, DIETARY; VITAMINS AND HEALTH.

nutritional assessment A clinical evaluation of an individual's nutritional status, typically as part of a ROUTINE MEDICAL EXAMINATION or as a direction of the diagnostic path when evaluating symptoms that suggest NUTRITIONAL DEFICIENCY, MALNUTRITION, gastrointestinal disorders, and systemic (body-wide) disease. Routine nutritional assessment is particularly important for the very young and the very old.

A nutritional assessment begins with measurement of height and body weight; physical examination to detect any signs or indications of nutritional deficiency; and a discussion of the person's EATING HABITS, including the kinds and amounts of food consumed over the course of a day or a week. Basic BLOOD tests can measure the levels of key NUTRIENTS in the blood circulation or nutrients the doctor suspects are deficient (such as iron). The doctor may conduct further tests, depending on the person's health circumstances.

The doctor may also measure UPPER ARM CIRCUMFERENCE, TRICEPS SKINFOLD, WAIST CIRCUMFERENCE, and hip circumference, factors that allow the doctor to quantifiably assess BODY FAT PERCENTAGE as well as loss of MUSCLE tissue in suspected nutritional disorders. From these measurements the doctor or nutritionist can calculate BODY MASS INDEX (BMI), basal metabolic rate (BMR), resting metabolic rate (RMR), and anticipated daily CALORIE requirements based on the person's lifestyle, weight management needs, and unique health circumstances.

See also AGING, NUTRITION AND DIETARY CHANGES THAT OCCUR WITH; DIET AND HEALTH; EXERCISE AND HEALTH; METABOLISM.

nutritional deficiency Inadequate consumption of one or more key NUTRIENTS. Gastrointestinal disorders of MALABSORPTION, such as CELIAC DISEASE and INFLAMMATORY BOWEL DISEASE (IBD), also cause nutritional deficiencies. Long-term, chronic health conditions or their treatments place extended demands on the body's nutrient base. Certain medications may interfere with how the body absorbs or maintains nutrients, such as diuretics ("water pills") which alter the body's mechanisms for retaining magnesium, sodium, potassium, and calcium.

Other treatments such as RENAL DIALYSIS for RENAL FAILURE may remove nutrients from the body. As well, people who have chronic health conditions are not always able to eat properly and thus do not consume adequate nutrients. Vitamin and mineral (micronutrient) deficiencies may develop in people who voluntarily limit their food intake to certain kinds of foods, such as those who follow strict vegan (no animal protein) diets. Fad diets may lead to deficiencies of macronutrients, most commonly protein.

HEALTH CONDITIONS AND CIRCUMSTANCES THAT CAN CAUSE NUTRITIONAL DEFICIENCIES

ALCOHOLISM	anorexia nervosa
BARIATRIC SURGERY	CELIAC DISEASE
COMA	CYCLIC VOMITING SYNDROME
GASTRECTOMY	INFLAMMATORY BOWEL DISEASE (IBD)
MALABSORPTION	PEPTIC ULCER DISEASE
PERSISTENT VEGETATIVE STATE	RENAL DIALYSIS
SHORT BOWEL SYNDROME	STARVATION

Deficiencies are most likely to occur with water-soluble nutrients as the body's stores of these are short-term. Though prompt intervention through dietary changes and nutritional supplementation can easily reverse most nutritional deficiencies, unresolved or untreated nutritional deficiencies can result in serious health conditions such as SCURVY (vitamin C deficiency) and OSTEOPOROSIS (calcium deficiency).

See also DIET AND HEALTH; HEMOCHROMATOSIS; MALNUTRITION; NUTRITIONAL SUPPLEMENTS; WILSON'S DISEASE.

nutritional needs The kinds and amounts of NUTRIENTS the body needs to maintain itself in good health. Research has established minimum levels of many nutrients, and health experts make recommendations for others based on the best available information. The roles of some nutrients remain poorly understood, though the body appears to require the nutrients for proper functioning. A person's nutritional needs change with life stage, lifestyle, PREGNANCY, and health circumstances.

Acknowledging the individualized nature of nutritional needs, the US Department of Agriculture (UDSA), the government agency responsible for establishing guidelines and standards for nutrition and diet, in 2005 revised its gold standard food guide pyramid to present 12 models of recommendations. The different models allow individuals to customize food choices to meet their physical needs and health circumstances, emphasize variety, and incorporate recommendations for

NUTRIENT DEFICIENCIES AND THEIR POTENTIAL HEALTH PROBLEMS

Deficient Nutrient	Health Conditions
calcium	OSTEOMALACIA, OSTEOPOROSIS, RICKETS
	MUSCLE cramps
	HEART ARRHYTHMIA
	HYPERTENSION (high BLOOD PRESSURE)
	insomnia
chromium	GLUCOSE intolerance
	peripheral NEUROPATHY
copper	slow HEALING

Deficient Nutrient	Health Conditions
fluorine (fluoride)	DENTAL CARIES (cavities)
iodine	GOITER HYPOTHYROIDISM
iron	iron-deficiency ANEMIA delayed growth and development in children GLOSSITIS (reddened, swollen, painful tongue)
phosphate	BONE DENSITY loss, osteoporosis
selenium	may contribute to hypothyroidism increased susceptibility to certain viral infections
vitamin A	NIGHT BLINDNESS hardening (keratinization) of tissue within the internal organs reduced resistance to INFECTION
vitamin B complex	BERIBERI PELLAGRA pernicious anemia, megaloblastic anemia PARESTHESIA (disturbances of sensory perception) DEPRESSION cognitive dysfunction fatigue, weakness
vitamin C	SCURVY slow healing gum disease, tooth loss
vitamin D	RICKETS, osteomalacia, osteoporosis
vitamin E	hemolytic anemia RETINOPATHY of prematurity ATAXIA, coordination difficulties, muscle weakness, paresthesia
VITAMIN K	easy bruising and bleeding COAGULATION disorders deficits of CLOTTING FACTORS
zinc	ALOPECIA (HAIR loss) HYPOGONADISM night blindness slow healing, lowered resistance to infection loss of APPETITE, altered sense of taste chronic DERMATITIS

physical exercise. Interactive food guide pyramid models are accessible at the USDA's Web site (www.mypyramid.gov). The USDA publication *Dietary Guidelines for Americans 2005* includes discussion of the food guide pyramids and other nutritional information.

Since the 1940s the standard of appropriate nutritional intake for individual nutrients has been the recommended dietary allowance (RDA), which quantifies how much of a nutrient a person should consume to prevent deficiency of that nutrient. Through the decades since, new knowledge and understanding have resulted in the emergence of additional standards that attempt to quantify the normal levels of nutrients necessary for health as well as the lower and upper limits beyond which health problems arise. These now fall collectively under the umbrella term *dietary reference intake (DRI)*. Because most people do not consume the "daily" amount of a nutrient every day the DRI system also takes into consideration variations in eating patterns and nutrient consumption, using formulas that look at nutritional needs over the long term and establishing averages that meet them.

For further discussion of nutritional needs, please see the overview section "Nutrition and Diet."

See also AGING, NUTRITION AND DIETARY CHANGES THAT OCCUR WITH; ANTIOXIDANT; LIFESTYLE AND HEALTH; MINERALS AND HEALTH; VITAMINS AND HEALTH.

nutritional supplements Products that provide additional NUTRIENTS and dietary substances beyond those that enter the body via food consumption. The most commonly taken nutritional supplements, also called dietary supplements, are vitamins and minerals, which are available in combination formulas (multivitamin supplements, multimineral supplements, and multivitamin with mineral supplements) as well as products that contain single nutrients. Some products combine vitamins and minerals with herbal and botanical substances, for example vitamin C with ECHINACEA. The choices among products are nearly endless; the nutritional supplement industry remains a key player in the American economy, with annual sales exceeding $19 billion.

In the United States federal law classifies vitamin and mineral supplements and most MEDICINAL HERBS AND BOTANICALS as dietary supplements. This removes these products from the jurisdiction of the US agency charged with oversight of DRUG safety and EFFICACY, the US Food and Drug Administration (FDA). Though various federal laws regulate matters of safety and efficacy as well as advertising claims of health benefits, testing of supplement products shows wide variation of quality standards across manufacturers and products. This can result in inconsistent doses and effectiveness.

The intent of nutritional supplements should be to augment, not replace, dietary nutrients. Vitamins, minerals, and botanicals do not deliver energy nutrients, though other kinds of nutritional supplements (such as protein supplements) do. Health experts disagree on whether the effect of supplements, especially vitamins and minerals, in the body is the same as that when the same nutrients enter the body from food sources. Some research studies investigating antioxidants, for example, show much higher levels of activity from consumed foods compared to supplements. Other studies show no measurable difference. A common philosophy among nutritionists is "stay close to the earth" because the highest concentrations of nutrients come from fresh fruits, vegetables, and whole grains.

People who have chronic health conditions or take regular prescription medications should check with the doctor or pharmacist before taking nutritional supplements of any kind, as the risk for DRUG INTERACTION is high. As well, some chronic health conditions or the medications taken to treat them have specific effects on how the body absorbs and metabolizes nutrients, increasing or decreasing the need for those nutrients. For such people, doctors may recommend therapeutic nutritional supplementation. For others, most health experts recommend obtaining nutrients from the diet to the extent possible and using nutritional supplements, including vitamins and minerals, only when there are clear and specific reasons to supplement dietary intake. However, research continues to generate new knowledge and understanding of how nutrients affect health

and disease, and recommendations continue to evolve. Many people integrate specific nutritional supplements with healthy EATING HABITS.

See also ANTIOXIDANT; MINERALS AND HEALTH; NUTRITIONAL DEFICIENCY; NUTRITIONAL THERAPY; VITAMIN AND MINERAL THERAPY; VITAMINS AND HEALTH.

P–R

parenteral nutrition The intravenous administration of NUTRIENTS as a method of supplying appropriate sustenance to a person who cannot meet his or her NUTRITIONAL NEEDS by eating, such as someone who is in a COMA or has a severe swallowing disorder. Parenteral nutrition, called total parenteral nutrition (TPN) when it is a person's sole source of nutrition, is helpful for short-term, intense feeding when ENTERAL NUTRITION is not a viable option. Parenteral nutrition is most successful as temporary supportive treatment such as after extensive surgery or during recovery from major trauma, though sometimes is necessary for longer therapy such as in severe gastrointestinal disease or cancer. In the long term, however, parenteral nutrition cannot deliver all of the nutrients the body needs and, in particular, is lacking in its ability to supply lipids (fats), which the body requires for cell maintenance and energy.

Parenteral nutrition solutions are very irritating to the veins so must be infused into the larger veins deep in the chest. This requires the doctor to insert a percutaneous intravenous catheter (PIC line) into a VEIN in the arm and thread it through the smaller vein to a large vein. An alternative is a Hickman line, in which the intravenous catheter enters the jugular vein at the base of the neck and extends into the superior VENA CAVA, the largest vein in the upper body. Fluids run continuously into either line with the aid of an infusion pump to maintain delivery of the solution at constant rate and pressure.

Some of the complications of extended parenteral nutrition include LIVER FAILURE, RENAL FAILURE, NUTRITIONAL DEFICIENCY (notably of trace minerals and lipids), and MALNUTRITION. INFECTION is also a significant risk, partly because the indwelling catheter provides a pathway for BACTERIA to enter the body and partly because the content of parenteral nutrition solutions is very high in GLUCOSE, which attracts and feeds bacteria.

See also END OF LIFE CONCERNS; QUALITY OF LIFE; SWALLOWING DISORDERS.

pellagra A health condition resulting from long-term deficiency of niacin (vitamin B_3). Pellagra is uncommon in the United States, occurring primarily in people who have chronic ALCOHOLISM or gastrointestinal disorders that prevent absorption of dietary niacin (also called niacinamide, nicotinamide, nicotinic acid, or niacinic acid) or of the essential amino acid tryptophan. The body requires niacin for cellular METABOLISM. Tryptophan is a niacin precursor from which the body can synthesize niacin. Niacin is necessary for the energy conversions that take place during cellular metabolism.

Symptoms and Diagnostic Path

Early symptoms of pellagra are those of nonspecific gastrointestinal upset: NAUSEA, VOMITING, and DIARRHEA. Burning in the MOUTH and especially of the tongue is common, with a characteristic gray membranous tissue coating on the gums that continually sloughs or peels. As pellagra worsens, additional symptoms that appear include GLOSSITIS (inflamed tongue) and SKIN RASH that intensifies with sun exposure after which the skin becomes rough, thick, and discolored. A characteristic pattern of this damage often develops around the neck.

At the same time, the lack of niacin causes the mucosa (mucous membrane lining) of the gastrointestinal tract to deteriorate, progressively reducing the ability of the intestines to absorb nutrients; MALNUTRITION results. Niacin deficiency

also affects neurons (NERVE cells) and the functioning of the CENTRAL NERVOUS SYSTEM, resulting in behavioral disturbances, delusions, confusion, and DEMENTIA. Disturbances of neuromuscular function include rigidity and involuntary activation of reflexes. The diagnostic path includes BLOOD tests to measure the levels of niacin and tryptophan in the blood circulation. The diagnosis is primarily clinical, however, based on the presenting symptoms and their response to treatment with niacin supplementation.

Treatment Options and Outlook

Treatment is immediate supplementation with niacin, usually in the form of niacinamide, and correction of EATING HABITS to restore foods to the diet that provide niacin. At therapeutic doses niacin often causes uncomfortable symptoms such as SKIN flushing and tingling; the niacinamide form, a slightly different chemical structure, does not. Both chemical forms provide the body with the niacin the cells need for energy conversion. Though many of pellagra's symptoms are reversible, those affecting the skin often result in permanent changes that are sometimes disfiguring. Untreated pellagra results in multisystem organ failure that is usually fatal.

Risk Factors and Preventive Measures

Pellagra develops as a consequence of niacin deficiency; thus adequate niacin intake prevents pellagra. Most people can obtain sufficient niacin supplies through the foods they eat. Meats, poultry, and other animal-based proteins contain high amounts of tryptophan, which the body converts to niacinamide. Asparagus, mushrooms, potatoes, spinach, peanuts and peanut butter, and legumes contain high amounts of niacin.

People who eat large quantities of corn and foods made with corn flour and who do not eat other kinds of foods, are at high risk for pellagra. The niacin in corn is not available through digestion. Other people at high risk for pellagra are those taking long-term treatment with isoniazid for TUBERCULOSIS or who have chronic CIRRHOSIS (the LIVER is fundamental in converting tryptophan to niacinamide).

See also ANEMIA; BERIBERI; DELUSION; NEURON; NUTRITIONAL DEFICIENCY; NUTRITIONAL NEEDS; RICKETS; SCURVY; VITAMINS AND HEALTH.

rickets A health condition that results from long-term deficiency of vitamin D, also called calciferol or ergocalciferol, in which the bones cannot absorb calcium or build new BONE tissue. The body makes most of the vitamin D it requires from cholesterol and sunlight. Dietary sources of vitamin D are primarily those that contain added supplements such as dairy products, orange juice, and some SOY-based food products. Cod liver oil naturally contains ergosterol, a form of vitamin D called D_2, as do oily fish such as salmon and sardines (though not in as high a concentration as cod liver oil). Supplemental vitamin D also interacts with cholesterol to form calcitriol.

The LIVER manufactures cholesterol, the base for vitamin D, and sends a certain amount for storage in the cells of the SKIN. Exposure to the sun's ultraviolet B (UVB) rays activates a series of chemical changes that convert the stored cholesterol molecules to a HORMONE form of vitamin D called calcitriol. The liver and the KIDNEYS also par-

PELLAGRA SYMPTOMS

Gastrointestinal	Dermatologic	Neurologic
DIARRHEA	bullae (blisters)	anxiety
GASTROINTESTINAL BLEEDING	erythema	DEMENTIA
GLOSSITIS	hyperpigmentation	DEPRESSION
loss of APPETITE	PHOTOSENSITIVITY	disorientation
MALABSORPTION	thickened SKIN	ENCEPHALOPATHY
NAUSEA		HALLUCINATION
stomatitis		irritability
VOMITING		PARANOIA

ticipate in these chemical changes. In combination with PARATHYROID HORMONE, calcitriol maintains a steady level of calcium in the BLOOD circulation. This balance allows the gastrointestinal tract to absorb calcium from dietary sources and the bones to accept calcium from the supply circulating in the blood.

Rickets develops when a long-term deficiency of vitamin D results in decreased dietary absorption of calcium. To meet its extensive needs for calcium, an important ion for numerous cellular functions, including proper contraction of the MUSCLE cells of the HEART, the body draws calcium from the bones. The bones demineralize and weaken. The long bones, notably those in the legs, bow. Doctors generally use the term *rickets* to refer to this disease process in children and the term OSTEOMALACIA to refer to this disease process in adults.

Symptoms and Diagnostic Path

The primary symptoms of rickets are bowed legs and a protruding belly (the result of weakened abdominal muscles). Deformities may develop at the epiphyses, or growth plates, of the bones, forming characteristic knobs and bumps. The diagnostic path includes X-rays to assess the density and mineralization of the bones and blood tests to measure the levels of calcium, phosphorus, and parathyroid hormone in the blood circulation. The doctor will also take a thorough PERSONAL HEALTH HISTORY including EATING HABITS.

Treatment Options and Outlook

Prompt vitamin D supplementation generally reverses most circumstances of mild to moderate rickets with little residual damage. Moderate to severe rickets, which is fairly uncommon in the United States, may result in consequential deformities of the pelvis, rib joints, and knee and ankle joints. Proper nutrition usually maintains adequate vitamin D intake.

Risk Factors and Preventive Measures

Most people will synthesize (make) all the vitamin D their bodies require with regular modest sun exposure, about 20 minutes to the face and arms four or five days a week. The farther from the equator a person lives, the longer sun exposure is necessary because the intensity of the sun's ultraviolet radiation diminishes. The ideal exposure is that which is just less than what results in mild SUNBURN. Doctors recommend multiple short exposures (5 to 15 minutes several times a day) to reduce the risk for sunburn. Applying sunscreen before going in the sun, though a prudent and recommended measure to prevent sun-related skin damage when engaging outdoor activities, prevents ultraviolet rays from penetrating the skin. People who have dark skin require longer periods of sun exposure.

Some health experts recommend that people who live in regions where the hours of sunlight drop below 12 hours a day (such as above 40 degrees latitude in the Northern Hemisphere, which includes locations north of the US cities San Francisco, Denver, St. Louis, Indianapolis, Philadelphia, and New York City) take vitamin D supplement. It is important to remain within the recommended dosage guidelines, however, because vitamin D is a fat-soluble vitamin that can accumulate in the body to reach toxic levels.

The antiseizure medication phenytoin increases the body's METABOLISM of calcidiol, one of the intermediary vitamin D forms. People who take this medication may need therapeutic vitamin D supplementation, particularly if they do not spend much time outdoors. Young children who live in inner city areas where smog is a problem have increased risk for rickets even when they spend time outdoors because the smog acts to filter the sun's ultraviolet rays.

See also ANEMIA; BERIBERI; FANCONI'S SYNDROME; MALNUTRITION; NUTRITIONAL DEFICIENCY; NUTRITIONAL NEEDS; PELLAGRA; SCURVY; VITAMINS AND HEALTH.

S–T

satiety The sensation of fullness and satisfaction after eating a meal. Satiety represents a convergence of physical, physiologic, and emotional factors. The physical sensation of fullness occurs when enough food fills the STOMACH to stretch its walls. The stretching activates NERVE and HORMONE sensors that then send physiologic signals to the APPETITE and satiety centers in the BRAIN and to receptors in the SMALL INTESTINE and the HUNGER center in the HYPOTHALAMUS. These signals slow or stop the release of hormones and neurotransmitters necessary for digestion and initiate the release of other hormones and biochemicals that have roles in absorbing NUTRIENTS into the BLOOD circulation and further METABOLISM of those nutrients.

Research indicates that foods high in protein result in reaching physical satiety the most rapidly. Foods high in fat take much longer to trigger physical satiety. These findings imply that eating the proteins in a meal first, such as meats or legumes, may curb the appetite, whereas eating the fats or carbohydrates in a meal first may extend appetite. Each circumstance has advantages, depending on an individual's health and weight management situation.

The emotional component of satiety comes when the meal has satisfied desires for certain characteristics of food such as textures, flavors, and quantity. Emotional satiety results in nerve signals to pleasure receptors in the cerebral cortex as well as to the brain's appetite and satiety centers. This is the most variable factor of satiety, influencing whether a person eats not enough or too much. Emotional eating is a significant dimension of WEIGHT LOSS AND WEIGHT MANAGEMENT.

See also EATING HABITS; FOOD CRAVINGS; NEUROTRANSMITTER.

scurvy A health condition that results from long-term deficiency of vitamin C (also called ascorbic acid). Vitamin C is essential for the formation of collagen, a fibrous protein that is the foundation for connective tissue throughout the body and the framework for BONE tissue. Collagen is integral to the walls of BLOOD vessels. Collagen also is an essential component of SCAR tissue, necessary for wound HEALING. Without vitamin C, a water-soluble vitamin the diet must provide on a relatively daily basis, the body cannot produce collagen.

Symptoms and Diagnostic Path

The most common symptoms of scurvy are bleeding gums and loose TEETH. Other symptoms include low grade FEVER, extended or lack of wound healing, PETECHIAE (pinpoint hemorrhages beneath the SKIN), and internal hemorrhage. ANEMIA is often the indication that there is bleeding somewhere in the body. The diagnostic path includes blood tests to measure the amount of ascorbic acid in the blood circulation as well as in the white blood cells (leukocytes) along with a careful PERSONAL HEALTH HISTORY that includes information about EATING HABITS.

Treatment Options and Outlook

Treatment for scurvy is vitamin C supplementation, which generally restores vitamin C levels and eliminates symptoms after about a week of treatment. In all but the most severe cases, scurvy is completely curable. Doctors generally recommend continued vitamin C supplementation to prevent RECURRENCE. Because vitamin C is water-soluble, there is no risk of toxicity with such prophylaxis. Increasing dietary consumption of foods that con-

tain vitamin C, notably raw fruits and vegetables, helps maintain adequate intake.

FOODS HIGH IN VITAMIN C

bell peppers (especially red)	broccoli
brussels sprouts	cabbage
cantaloupe	grapefruit
kiwi	lemons
limes	mango
oranges	spinach
strawberries	sweet potatoes
watermelon	

Risk Factors and Preventive Measures

Scurvy occurs only as a deficiency of vitamin C, thus adequate vitamin C consumption prevents scurvy. People who have increased risk for scurvy are those who have chronic ALCOHOLISM, chronic health conditions that interfere with the digestion or absorption of NUTRIENTS, and the very elderly who may not receive adequate nutrition through diet because they cannot or do not eat properly. Fruit and vegetable juices are easy substitutions for whole fruits and vegetables. Many juices are fortified with additional vitamin C and other nutrients.

See also BERIBERI; FANCONI'S SYNDROME; LEUKOCYTE; MALNUTRITION; NUTRITIONAL DEFICIENCY; NUTRITIONAL NEEDS; PELLAGRA; RICKETS; VITAMINS AND HEALTH.

starvation The most severe state of MALNUTRITION resulting from extended lack of food and nutrition. An otherwise healthy adult may lose up to 50 percent of body weight before organ systems fail and death occurs. Total starvation that persists beyond about 10 to 12 weeks is usually fatal. In the United States starvation most commonly occurs as a consequence of severe illness, severe gastrointestinal disease, prolonged COMA, and anorexia nervosa. In parts of the world where food supplies are limited, starvation results from famine and causes millions of deaths every year.

The body attempts to survive starvation by dramatically slowing METABOLISM. HEART RATE and BREATHING rate slow, BLOOD PRESSURE and body temperature drop, and BLOOD flow to nonvital structures diminishes. The body turns to tissues such as MUSCLE and most organs outside the CENTRAL NERVOUS SYSTEM, breaking them down into chemical products that it can use as NUTRIENTS. Consequently emaciation, in which the body looks gaunt and wasted, is a key characteristic of starvation.

Treatment for starvation is aggressive nutritional supplementation to restore the body to a state such that organ systems begin to function. It can take several weeks for the gastrointestinal system to be able to manage solid foods, during which time PARENTERAL NUTRITION can provide sustenance. ENTERAL NUTRITION can deliver concentrated nutrients to address emerging NUTRITIONAL DEFICIENCY disorders. Full recovery may take six months or longer, depending on what underlying health conditions exist.

See also EATING DISORDERS; NUTRITIONAL SUPPLEMENTS.

triglycerides, dietary Chemical structures that contain three fatty acids in combination with glycerol. Triglycerides are the most common forms of fat in foods and in the body. The body uses triglycerides primarily for energy. Dietary triglycerides circulate in the BLOOD along with triglycerides the LIVER synthesizes from carbohydrates and fats the body does not use for immediate energy. Some triglycerides then go to cells for use as energy and others go to adipose (fat) cells for storage.

The liver also uses dietary triglycerides to synthesize (make) lipoproteins, the carrier proteins that transport cholesterol and fats through the bloodstream to cells throughout the body. Low-density lipoproteins (LDLs) and very low-density lipoproteins (VLDLs) have higher levels of triglycerides than high-density lipoproteins (HDLs). Elevated levels of LDLs and VLDLs in the blood circulation correlate to increased risk for CARDIOVASCULAR DISEASE (CVD), HEART ATTACK, and STROKE.

Triglycerides are present in a wide range of foods, notably animal-based foods and oils and fats. Reducing overall food consumption so the calories in balance with the calories out and reducing the amount of refined carbohydrates (sugars) in the diet are the most effective way to reduce blood triglyceride levels. Daily physical exercise helps the body more efficiently metabolize nutrients and increases the consumption of triglycerides as an energy source. A small percentage of people have a

genetic disorder of lipid METABOLISM that causes them to have high amounts of triglycerides in their blood circulation. Lipid-lowering medications may then be necessary to bring triglycerides levels down.

See also CARDIOVASCULAR DISEASE PREVENTION; CHOLESTEROL, DIETARY; CHOLESTEROL BLOOD LEVELS; GENETIC DISORDERS; HYPERLIPIDEMIA; TRIGLYCERIDE BLOOD LEVEL.

V

vitamins and health Vitamins are organic micronutrients essential for health and the body's proper growth, development, and function. They interact with each other or with other biochemicals in the body, functioning as cofactors or coenzymes to carry out activities of energy conversion (METABOLISM) though do not themselves provide energy to the body. With the exception of vitamin D, dietary sources provide the vitamins the body requires.

There are 12 vitamins that are essential for health. The 8 B vitamins and vitamin C are water soluble; the body cannot stockpile stores of them (except in limited accumulations within the BLOOD circulation and the LIVER) and thus requires regular consumption to maintain levels adequate to support health. Most healthy people can obtain the vitamins their bodies need for normal functioning through dietary sources. Vitamins A, E, D, and K are fat soluble; the body stores excess amounts of these vitamins in adipose (fatty) tissue and draws from these supplies when dietary intake does not meet needs.

Vitamin deficiency may develop when dietary consumption is inadequate, as a result of gastrointestinal disorders that interfere with nutrient absorption or owing to interactions with medications. Chronic health conditions may drain the body of important NUTRIENTS, including vitamins. Untreated vitamin deficiency can cause potentially serious health conditions such as SCURVY, RICKETS, and NIGHT BLINDNESS.

Vitamin toxicity occurs most commonly as a consequence of excessive vitamin supplementation and can have serious or permanent consequences. Metabolic disorders and medications that interfere with vitamin metabolism are also common culprits. Vitamin toxicity is more common with the fat-soluble vitamins because they accumulate in the body. Vitamin toxicity also is possible with extreme overconsumption of water-soluble vitamins, usually the result of higher levels in the blood circulation than the body can excrete.

Vitamin toxicity is more likely to occur when taking a multiple vitamin supplement and individual supplements that supply significantly greater than the needed amounts of certain vitamins. Vitamins A; E; and the B vitamins niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), and folic acid (B_9) present the greatest risk for toxicity.

Vitamin A (Retinol)

Vitamin A is essential for proper functioning of the photoreceptor cells (rods and cones) of the RETINA, maintains the health of the SKIN, and appears to have some antiviral capabilities. It is also crucial for growth and development in children. The liver stores vitamin A, a fat-soluble vitamin, and releases it into the blood circulation as the body needs it. The primary dietary sources for vitamin A are foods that supply beta-carotene, which the body converts to retinol. Such foods include yellow vegetables and fruits, green leafy vegetables, egg yolks, and fish liver oil.

Vitamin A deficiency results in disturbances of vision, including impaired dark adaptation (slowing of the ability of the eyes to adjust to changes in lighting) and night blindness. In children, vitamin A deficiency can stunt growth and impair cognitive development. These developmental disruptions can have permanent consequences,

although vitamin A deficiency severe enough to cause such disruptions is rare. Other consequences of vitamin A deficiency generally improve when levels of vitamin A return to normal.

Vitamin A toxicity nearly always results from taking high doses of vitamin A supplement and can occur as acute OVERDOSE (taking an extremely large dose at one time) or chronic overdose (excess that accumulates over time), usually the result of oversupplementation. Treatment with retinol medications, such as for severe ACNE, also can result in vitamin A toxicity. In adults the effects and symptoms of vitamin A toxicity are reversible and generally resolve within a few weeks of stopping supplementation or therapeutic retinol.

Vitamin B Complex

The eight B vitamins, called the vitamin B complex, work in close synchronization with one another and have key roles in many functions in the body. Each B vitamin further has specific functions, dietary sources, deficiency level, and toxicity level. In general the B vitamins are essential for energy conversion (metabolism of carbohydrates and fats) and other functions of cellular metabolism, erythropoiesis (making new red blood cells), and maintaining the epithelium (skin and mucous membranes). The liver stores some of the B vitamins for a short time. Food sources of the B vitamins include meats, poultry, fish, eggs, leafy green vegetables, fruits, whole grains, brown rice, and fortified grain products such as cereals and breads (regulations in the United States require such fortification).

Deficiencies of B vitamins affect many functions of the body. Most often deficiencies of the B vitamins occur collectively, though specific deficiency disorders are BERIBERI (thiamine deficiency), PELLAGRA (niacin deficiency), and pernicious ANEMIA (cyanocobalamin deficiency). In the United States vitamin B deficiencies generally result from chronic health disorders, ALCOHOLISM, and MALABSORPTION disorders. In such circumstances it often is necessary for the person to take therapeutic vitamin B supplements, either B complex or specific B vitamins, to compensate.

Toxicity of B vitamins is uncommon though can occur when taking excessive vitamin supplements and in some metabolic disorders; it is most likely to develop with niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), and folic acid (B_9). Though most symptoms resolve when vitamin B intake returns to normal, vitamin B toxicities can result in permanent neurologic and skin damage.

Vitamin B_1 (thiamine) Thiamine converts carbohydrates into GLUCOSE and is a coenzyme in the synthesis of acetylcholine, a NEUROTRANSMITTER important for cognitive functions in the cerebral cortex and MUSCLE coordination throughout the body. Prolonged thiamine deficiency causes beriberi.

Vitamin B_2 (riboflavin) Riboflavin is a key player in macronutrient metabolism (fats, carbohydrate, and proteins) as well as in energy conversion at the cellular level (cellular oxidation). It is essential for growth and development in children, facilitates erythropoiesis (formation of new red blood cells), and helps support the health of the retina.

Vitamin B_3 (niacin) Niacin exists in two forms: nicotinic acid and niacinamide (also called nicotinamide). In either form it facilitates the metabolism of carbohydrates (glycolysis) and functions of cellular energy conversion. Niacin also helps maintain the structure of the epithelium (skin and mucous membranes). The body synthesizes some niacin from the essential amino acid tryptophan. Prolonged niacin deficiency causes pellagra. Niacin has emerged as an effective therapy for mild to moderate HYPERLIPIDEMIA, reducing CHOLESTEROL BLOOD LEVELS as effectively as some lipid-lowering medications.

Vitamin B_5 (pantothenic acid) Pantothenic acid is essential for metabolizing amino acids and fats to carbohydrates, and works in collaboration with folic acid and biotin for various functions related to cellular energy conversion. The liver uses pantothenic acid in the synthesis of hormones and cholesterol. Canning and freezing destroy pantothenic acid.

Vitamin B_6 (pyridoxine) Pyridoxine facilitates HEMOGLOBIN production, conversion of tryptophan to niacin, and carbohydrate metabolism. Other forms of vitamin B_6 are pyridoxal and pyridoxamine; all forms of vitamin B_6 convert to the coenzyme pyridoxal-5'-phosphate (PLP) in the body. Health conditions that increase the body's specific use of and need for pyridoxine include

alcoholism, END-STAGE RENAL DISEASE (ESRD) with RENAL DIALYSIS, serious BURNS, major surgery, GASTRECTOMY or BARIATRIC SURGERY, and chronic CIRRHOSIS. People who smoke and women who take oral contraceptives (birth control pills) are at high risk for pyridoxine deficiency.

Vitamin B_7 (biotin) Biotin works in close alliance with folic acid and pantothenic acid, and is important in metabolizing macronutrients, especially carbohydrates and fats, from food during digestion. Sulfa-based ANTIBIOTIC MEDICATIONS can prevent the body from absorbing biotin from foods during digestion.

Vitamin B_9 (folic acid) Folic acid, also called folate, is essential for the formation of new blood cells (HEMATOPOIESIS) and works in conjunction with cyanocobalamin to repair DNA. Folic acid is crucial for normal development of the neurologic system in the early EMBRYO; prophylactic folic acid decreases NEURAL TUBE DEFECTS by up to 80 percent. Folic acid also participates in cellular energy conversion cycles.

FOLIC ACID PREVENTS NEURAL TUBE DEFECTS

Folic acid is so effective at preventing NEURAL TUBE DEFECTS that doctors urge all women who could become pregnant, regardless of whether they are planning PREGNANCY and especially if they are taking oral contraceptives (which deplete folic acid), to take a folic acid supplement that delivers 400 micrograms daily. Folic acid is crucial for the closure of the neural tube, the rudimentary CENTRAL NERVOUS SYSTEM that develops in the EMBRYO about 14 days after CONCEPTION.

Vitamin B_{12} (cyanocobalamin) Cyanocobalamin, also called cobalamin, is essential for the formation of myelin, the protein coating that protects NERVE fibers. It also participates in DNA repair (nucleic acid synthesis), erythropoiesis (formation of new red blood cells), and folic acid metabolism. Intrinsic factor, which the stomach produces, is essential for absorption of cyanocobalamin. Health conditions that diminish intrinsic factor production, such as PEPTIC ULCER DISEASE, and circumstances such as bariatric surgery or gastrectomy, significantly reduce the body's ability to absorb cyanocobalamin and often require supplementation via vitamin B_{12} injections. The ability to produce intrinsic factor diminishes with age, increasing the risk of deficiency.

Vitamin C (Ascorbic Acid)

The body requires vitamin C to create collagen, a protein critical for the formation of connective tissue and in healing (the formation of scar tissue). Collagen forms the foundation of the SKELETON over which the bones develop. Vitamin C is also necessary for production of serotonin, a vital neurotransmitter, and aids in the dismantling of cholesterol for excretion in the BILE. The body absorbs significantly more iron in combination with vitamin C; health experts recommend eating combinations of foods that contain these substances and taking iron supplements with a glass of orange juice. Citrus fruits are the primary dietary source of vitamin C.

LIMEYS

British sailors of the 19th century acquired the nickname "limey" when the British Navy began including limes in sailors' rations while at sea. Citrus fruits are high in vitamin C, which prevents SCURVY. Limes hold up better in storage than other citrus fruits. Before this practice, half or more of a ship's crew often died before returning home from a long sea voyage.

Long-term vitamin C deficiency results in scurvy, a condition of collagen depletion with symptoms that affect the musculoskeletal, neurologic, and immune systems. Vitamin C deficiency is rare in modern times. Increasing dietary consumption of foods high in vitamin C is usually adequate to restore vitamin C levels and reverse symptoms. Though vitamin C is a water-soluble vitamin, it can accumulate to toxic levels with excessive supplementation. The symptoms of vitamin C toxicity (NAUSEA, DIARRHEA, and sometimes anemia) improve immediately when vitamin C consumption returns to normal.

Vitamin C is also a powerful ANTIOXIDANT with roles in healing and preventing diseases. Much research has explored these roles in recent decades, and numerous studies support vitamin C's ability to expedite recovery from viral infections such as COLDS (though vitamin C cannot prevent such infections). Doctors may recommend

vitamin C supplementation for people recovering from major surgery, serious burns, and significant dental procedures.

Vitamin D (Calciferol)

Without vitamin D, the body cannot use calcium. Vitamin D is unique among vitamins in that the body can manufacture it as a process of photosynthesis (exposure to sunlight) that converts a form of cholesterol stored in the cells of the skin into vitamin D. Only a small portion of vitamin D enters the body from dietary sources (namely, fortified dairy products) in the form of vitamin D_2 (ergocalciferol) or vitamin D_3 (cholecalciferol). The circulating, active form of vitamin D is calcitriol, which functions as a HORMONE. Calcitriol, in tandem with PARATHYROID HORMONE, regulates the amount of calcium in the blood. This regulation determines the availability of calcium to the bones. Vitamin D also influences IMMUNE SYSTEM functions important for fighting tumors.

Vitamin D deficiency affects bone structure, preventing bone tissue from accepting new calcium and allowing calcium to leave the bones to enter the blood circulation. Vitamin D deficiency can cause rickets in children and OSTEOMALACIA in adults. Both are conditions of demineralization that are reversible with vitamin D supplementation, though severe rickets may result in residual deformity particularly of the pelvis. Sustained vitamin D deficiency in adults leads to OSTEOPOROSIS, an irreversible loss of bone tissue.

Vitamin D toxicity may develop with excessive consumption from vitamin supplements, which can be supplementation within normal limits in healthy people who get adequate vitamin D from dietary sources and is a particular risk among people who take megavitamins. The toxic level is fairly low. Vitamin D toxicity is also a risk in people who are receiving treatment for HYPOPARATHYROIDISM. Excessive levels of vitamin D affect calcium reabsorption in the kidney (HYPERCALCEMIA) and often cause kidney stones (NEPHROLITHIASIS) that can result in permanent damage to the KIDNEYS.

Vitamin E (Tocopherol)

A fat-soluble vitamin, vitamin E's most important function is as an antioxidant. It blocks the reaction of free radicals to produce more free radicals and some metabolism of fatty acids. Vitamin E also maintains the integrity of erythrocytes (red blood cells), which are vulnerable to damage, in the blood circulation. Though vitamin E has a reputation for a wide range of actions in the body to prevent diseases such as cancer and CARDIOVASCULAR DISEASE (CVD); to treat conditions such as FIBROCYSTIC BREAST DISEASE; and to enhance physical ENDURANCE, LIBIDO, and reproduction, research has thus far failed to support these claims. Some research suggests that excessive amounts of vitamin E may in fact contribute to the development of certain cancers. Much research remains under way to better understand the roles of vitamin E in health and in disease.

Vitamin E deficiency may occur in disorders of fat absorption or metabolism though is quite rare. When present vitamin E deficiency may result in hemolytic anemia. Vitamin E toxicity is also uncommon and nearly always occurs in people who take excessive amounts of vitamin E supplements. Vitamin E toxicity can have deleterious effects on the mechanisms of COAGULATION, leading to hemorrhage.

Vitamin K (Quinone)

BACTERIA in the SMALL INTESTINE synthesize 80 percent or more of the VITAMIN K the body needs and uses. The other 20 percent comes from plant-based foods, notably spinach, broccoli, and other dark green vegetables. The bacterial form of vitamin K is menaquinone; the plant form of vitamin K is phylloquinone. Vitamin K is essential for the activation of several CLOTTING FACTORS (VII, IC, X) and prothrombin, which regulate the blood's ability to clot.

Vitamin K deficiency may occur in disorders that interfere with the absorption of fats into the body, such as GALLBLADDER DISEASE and gastrointestinal malabsorption disorders. Long-term antibiotic therapy can significantly reduce the bacteria count in the small intestine, restricting the body's ability to synthesize vitamin K. Anticoagulant medications such as warfarin work by blocking the action of vitamin K. Untreated vitamin K deficiency can result in life-threatening hemorrhage. Vitamin K toxicity is rare and occurs nearly always when taking vitamin K supplements. It can cause JAUNDICE and, when severe, permanent BRAIN damage. Some multivitamin supplements

ESSENTIAL VITAMINS AND THEIR DIETARY SOURCES

Vitamin	Dietary Sources
A (retinol)	carrots butternut squash, acorn squash, pumpkin spinach, turnip greens, chard broccoli mangos beef liver
B_1 (thiamine)	fortified breads and cereals pork, beef, ham, chicken, turkey, fish, eggs brewer's yeast dairy products legumes peas, corn, green beans, potatoes (with skins)
B_2 (riboflavin)	fortified breads and cereals dairy products pork, beef, ham, chicken, turkey, liver, fish, eggs oysters, clams, shrimp mushrooms
B_3 (niacin)	fortified breads and cereals dairy products pork, beef, ham, chicken, turkey, liver, eggs tuna, cod, halibut, bluefish, shrimp peas, corn, sweet potatoes, potatoes (with skins), spinach, broccoli peanuts
B_5 (pantothenic acid)	fortified breads and cereals mushrooms broccoli avocados
B_6 (pyridoxine)	fortified breads and cereals potatoes (with skin) bananas, apples, oranges, watermelon, grapefruit and grapefruit juice, avocados, prunes and prune juice legumes pork, beef, ham, chicken, turkey, liver, fish (especially tuna), eggs seeds, nuts, peanut butter
B_7 (biotin)	fortified breads and cereals brown rice, barley, oatmeal, whole wheat SOY products cauliflower egg yolks, liver tuna, finfish

contain vitamin K; unless a doctor specifically recommends vitamin K supplementation, however, most people should not take supplements that contain vitamin K.

See also CONTRACEPTION; MINERALS AND HEALTH; NUTRITIONAL SUPPLEMENTS; NUTRITIONAL THERAPY; VITAMIN AND MINERAL THERAPY.

Vitamin	Dietary Sources
B_9 (folic acid)	fortified breads and cereals spinach, okra, greens asparagus, broccoli, corn, green beans, sweet potatoes, potatoes (with skins) tomatoes and tomato juice legumes tofu seeds, nuts, peanut butter eggs
B_{12} (cyanocobalamin)	fortified breads and cereals pork, beef, ham, chicken, turkey, liver, fish, eggs shrimp, oysters, clams dairy products
C (ascorbic acid)	citrus fruits and juices: oranges and orange juice, lemons, limes, grapefruit and grapefruit juice watermelon, strawberries, cantaloupe papaya, mangos, tangerines, guava broccoli, kohlrabi, cabbage, cauliflower spinach, greens bell peppers
D (calciferol)	sunlight fortified dairy products, orange juice, and soy milk
E (tocopherol)	polyunsaturated oils egg yolks spinach, greens almonds, walnuts, pecans, cashews peanuts and peanut butter seeds (sunflower, flax) whole grains and whole grain products wheat germ
K (quinone)	spinach, lettuce other than iceberg broccoli, cabbage, kale, kohlrabi alfalfa (especially sprouts), oats, rye, whole wheat and whole wheat products

FITNESS: EXERCISE AND HEALTH

Exercise has emerged as a significant factor in nearly all facets of health, both in terms of maintaining overall health and in reducing risk for health conditions and injuries. A health-care practitioner who specializes in fitness-related care may be a doctor (MD or DO), certified physician assistant (PA-C), registered physical therapist (RPT), chiropractor (DC), or exercise physiologist. Doctors who specialize in treating injuries and conditions related to physical activity may be board-certified in sports medicine, family practice, orthopedics, or physiatry (rehabilitation medicine). Education, certification, and credentialing are less consistent for other fitness practitioners such as fitness trainers and athletic trainers who primarily work outside the health-care delivery system to help individuals develop exercise regimens for preventive or therapeutic purposes.

This section, "Fitness: Exercise and Health," presents an overview discussion of physical activity as it relates to health maintenance, health risk factors, health conditions, and preventive health measures. The entries in this section focus on the broad picture of how physical activity and inactivity influence health and disease. The section "Lifestyle: Obesity and Smoking" features discussion and entries about fitness and exercise topics that relate to WEIGHT LOSS AND WEIGHT MANAGEMENT. The section "The Musculoskeletal System" contains discussion and comprehensive entries about the structure, function, health, and health conditions of the bones, muscles, and joints.

Making the Connection between Physical Activity and Health

Researchers provided the first substantive correlation between physical inactivity and health in the 1970s when clinical and epidemiologic studies linked sedentary lifestyle with premature death due to health conditions such as CORONARY ARTERY DISEASE (CAD) and HYPERTENSION (high BLOOD PRESSURE). Health experts subsequently issued the first formal recommendations for incorporating regular physical exercise into daily lifestyle as a means of preventing the development of CARDIOVASCULAR DISEASE (CVD). These recommendations were much the same as current recommendations for minimal physical activity for adults, which are

- physical activity for a total of 30 minutes a day at moderate intensity at least 5 days a week and preferably every day
- physical activity for 20 minutes at a time at vigorous intensity on 3 or more days of the week

Research has continued to strengthen the evidence for these recommendations. However, most Americans fall short of meeting them. The 1996 US Surgeon General's report *Physical Activity and Health* found that 25 percent of Americans do not participate in any physical activity beyond the requirements of daily living, and 60 percent exercise less than the minimum recommendations for health. Among youth between the ages of 12 and 21, about 25 percent engage in physical activity at a level that meets minimum recommendations for health, 50 percent participate in regular physical activity at vigorous intensity, and 25 percent are physically inactive.

Many adults start exercise programs and then do not continue them, most commonly because they begin with activities that support the FITNESS LEVEL they want to achieve rather than those geared to their current fitness level. Such an approach often results in discomforts; minor injuries such as blisters, sore muscles, and aching joints; and discouragement because the body is not ready for such activity. It is important to start at the current fitness level and steadily work up to

the desired fitness level. The health benefits of exercise become apparent within two weeks of starting an exercise regimen and progress as physical activity continues. Conversely, the health benefits of physical activity diminish significantly two weeks after stopping an exercise regimen and are gone after two months of physical inactivity.

Though the overall health benefits of exercise far outweigh the risks, a few health risk factors do increase with physical activity, notably those for exercise-related injuries and REPETITIVE MOTION INJURIES. However, most such injuries are preventable through proper WARMUP, preparation, protective items, and technique during activity. Furthermore, maintaining a high fitness level reduces the risk for many other kinds of injuries because regular exercise increases BONE DENSITY, MUSCLE STRENGTH, FLEXIBILITY, and balance.

HEALTH RISKS ASSOCIATED WITH EXERCISE

ACHILLES TENDON INJURY	ANKLE INJURIES
BLISTER	CHAFING
CHARLEYHORSE	EPICONDYLITIS
FRACTURE	KNEE INJURIES
MUSCLE and JOINT soreness	ROTATOR CUFF IMPINGEMENT SYNDROME
SHIN SPLINTS	SYNOVITIS
SPRAINS AND STRAINS	
TENDONITIS	

Prescription: Exercise

Until the 1970s bedrest was the standard prescription for convalescence after significant health conditions ranging from herniated disk (HERNIATED NUCLEUS PULPOSUS) and KNEE INJURIES to HEART ATTACK and major surgical operations. Rest, according to prevailing medical wisdom, allowed the body to heal itself. With the collection of evidence of physical inactivity's harmful effects on health in general growing in the late 1960s, doctors began to question the value of the "rest to recover" approach and to implement gradual physical activity as part of a person's recuperation plan. Doctors observed that people who engaged in limited physical active early in the course of their recovery, such as sitting in a chair or walking to the bathroom, in the days immediately after an OPERATION or a heart attack improved faster and felt better than those who remained on bedrest. Doctors also noted that early mobility, now a mainstay of recuperation, reduced PULMONARY EMBOLISM (PE) and DEEP VEIN THROMBOSIS (DVT)—BLOOD clots in the LUNGS and the inner veins of the legs, respectively—which are risks with surgery and major injury.

By the mid-1980s supervised and graduated physical activity was the core of structured cardiac rehabilitation programs, and today exercise is a component of treatment regimens for numerous health conditions. Structured physical rehabilitation programs are now also the standard of care for people who have musculoskeletal injuries, operations, and conditions. The typical multidisciplinary health-care team includes professionals who specialize in returning the body to optimal function.

HEALTH CONDITIONS INFLUENCED BY PHYSICAL ACTIVITY AND INACTIVITY

ASTHMA	ATHEROSCLEROSIS
ATHLETIC INJURIES	BREAST CANCER (certain forms)
CARDIOVASCULAR DISEASE (CVD)	CHRONIC FATIGUE SYNDROME
CHRONIC PULMONARY OBSTRUCTIVE DISEASE (COPD)	COLORECTAL CANCER
CORONARY ARTERY DISEASE (CAD)	CONSTIPATION
DIABETES	DEPRESSION
HYPERLIPIDEMIA	FIBROMYALGIA
INSULIN RESISTANCE	HYPERTENSION
OBESITY	INTERMITTENT CLAUDICATION
OSTEOPOROSIS	OSTEOARTHRITIS
PROSTATE CANCER	PERIPHERAL VASCULAR DISEASE (PVD)

Fitness for Health: Public Health Goals

The US federal government adopted formal interest in and support for physical fitness in the 1950s, when President Dwight D. Eisenhower (1890–1969) formed the President's Council on Youth Fitness in response to published scientific data that America's youth were significantly less physically fit compared to European youth. Each US president after Eisenhower strengthened and broadened the role of government agencies to study exercise and educate the public about the relationship between EXERCISE AND HEALTH.

Through the 1970s and 1980s these initiatives expanded to encourage extended physical fitness and sports activities in the schools and support businesses and corporations in promoting exercise and fitness programs and opportunities among

employees. Health agencies such as the National Institutes of Health (NIH) and health organizations such as the American Heart Association (AHA) and the American Diabetes Association (ADA) espoused exercise and fitness as preventive measures as well as adjuncts for clinical treatment regimens. In 1990 and in 2000 the US Centers for Disease Control and Prevention (CDC) the US government's health promotion and prevention agendas for Americans, the Healthy People 2000 and HEALTHY PEOPLE 2010 initiatives, incorporated daily physical activity for youth and adults among their priority areas with the overriding objective of preventing health conditions and reducing overall premature deaths that result from physical inactivity.

KEY HEALTHY PEOPLE 2010 PHYSICAL ACTIVITY GOALS

- Reduce the proportion of adults who engage in no leisure-time physical activity.
- Increase the proportion of adolescents and adults who engage regularly, preferably daily, in moderate physical activity for at least 30 minutes per day.
- Increase the proportion of adolescents and adults who engage in vigorous physical activity that promotes the development and maintenance of cardiorespiratory fitness three or more days per week for 20 or more minutes per occasion.
- Increase the proportion of adults who perform physical activities that enhance and maintain muscular STRENGTH and ENDURANCE.
- Increase the proportion of adults who perform physical activities that enhance and maintain FLEXIBILITY.
- Increase the proportion of US public and private schools that require daily physical education for all students.
- Increase the proportion of work sites offering employer-sponsored physical activity and fitness programs.
- Increase among children, adolescents, and adults the proportion of trips made by walking.
- Increase among children, adolescents, and adults the proportion of trips made by bicycling.

A–B

aerobic capacity The maximum amount of oxygen the body can extract from ambient air (the air of the normal environment) and use during physical activity, expressed as $\dot{V}O_{2max}$ in terms of milliliters of oxygen per kilogram of body weight per minute (mL/kg/min). Because men have larger LUNGS and thus greater surface area for oxygen exchange, all other factors being equal men have greater aerobic capacity than women. Higher $\dot{V}O_{2max}$ correlates with increased ability to sustain high-intensity exercise for an extended time, such as during ENDURANCE activities. People who participate in athletic events at a competitive level, amateur or professional, typically have higher aerobic capacity in general and a significantly higher $\dot{V}O_{2max}$ in the activity of specialty such as bicycling, cross-country skiing, distance running, and swimming. Aerobic capacity is a key indicator of cardiovascular fitness.

REPRESENTATIVE AEROBIC CAPACITY MEASUREMENTS ($\dot{V}O_{2MAX}$)

sedentary woman	38 milliliters per kilogram per minute (mL/kg/min)
aerobically fit woman	60 mL/kg/min
sedentary man	42 mL/kg/min
aerobically fit man	80 mL/kg/min

Researchers believe the foundation of aerobic capacity is genetic; some people are born with greater aerobic capacity potential, and with sustained AEROBIC EXERCISE at a competitive level they are able to maximize that potential for high $\dot{V}O_{2max}$. A sedentary (physically inactive) person who undertakes a planned, progressive program of aerobic exercise can often improve his or her aerobic capacity by 20 to 30 percent. Such improvement is significant from a health perspective because there is a strong correlation between low aerobic capacity and increased risk for CARDIOVASCULAR DISEASE (CVD). Increasing aerobic capacity consequently lowers CVD risk factors.

Direct measurement of $\dot{V}O_{2max}$ is fairly complex; because of this doctors tend to conduct direct aerobic capacity testing only in people who have pulmonary disease. A pulmonary function testing center conducts direct $\dot{V}O_{2max}$ measurement, for which the person runs on a treadmill or rides a stationary bicycle wearing specialized equipment that measures the exchange of oxygen and carbon dioxide. Calculations using the measurements determine the $\dot{V}O_{2max}$, usually along with other measures that provide a detailed perspective of lung function and lung capacity.

There are several methods for indirectly measuring aerobic capacity, all of which involve performing sustained aerobic exercise such as running or walking for a determined period of time or a known distance. Calculations use the information to project the anticipated $\dot{V}O_{2max}$ for the data. Indirect $\dot{V}O_{2max}$ measurement is less precise than direct $\dot{V}O_{2max}$ measurement but is accurate enough for most people who are engaged in aerobic exercise and want to know, or monitor improvements in, their aerobic capacity.

See also FITNESS LEVEL.

aerobic exercise Physical activity that raises the HEART RATE to 60 percent of maximum heart rate, called the target heart rate, for a minimum continuous time of 20 minutes.

A general guideline for approximating one's target heart rate is the "talk test." At target heart rate, a person should be able to speak. A person who cannot talk during exercise is likely exceeding his or her target heart rate and is working too

hard. A person who can carry on an extended conversation or sing during exercise is likely below his or her target heart rate and is not working hard enough for aerobic conditioning.

CALCULATING TARGET HEART RATE

The standard formula for calculating target HEART RATE is 220 minus one's age (an estimated maximum heart rate), then multiplying the result by 60 percent. For example, the target heart rate for a person 35 years old is 111 beats per minute: 220 – 35 = 185 x 0.6 = 111.

Aerobic exercise uses the large MUSCLE groups in rhythmic, repetitive activity that increases the body's consumption of oxygen, and is the core of cardiovascular CONDITIONING. Regular aerobic exercise improves the all-around efficiency of the cardiovascular system including

- more powerful contractions of the HEART to pump BLOOD out to the body
- the ability of the LUNGS to exchange carbon dioxide for oxygen
- the ability of the muscles in the body to contract with power and force
- the ability of the blood vessels to dilate (open) to carry more blood with each beat of the heart
- lower BLOOD PRESSURE as a result of reduced resistance to the flow of blood

Health experts recommend a minimum of 30 minutes of aerobic exercise three days every week and encourage more. At the onset of an aerobic exercise program a person is likely to achieve target heart rate quickly because the heart is not accustomed to working in such a way. It is important to stay at the target heart rate for as long as possible, which may not be a full 20 minutes at first. As the FITNESS LEVEL and AEROBIC CAPACITY improve, it takes longer to reach and becomes easier to maintain one's target heart rate.

People who want to increase their fitness levels should increase both the length and frequency of their exercise sessions, for example 45 minutes of aerobic activities five days a week. The higher a person's aerobic capacity, the more effort the person must exert to achieve and maintain his or her target heart rate. Competitive athletes and people at high aerobic capacity may derive greater benefit from exercising at a target heart rate that is 70 to 80 percent of maximum heart rate.

Among the most familiar and popular aerobic activities are running, swimming, cross-country skiing, and bicycling. Brisk walking (five miles per hour) is aerobic as well. Sports such as basketball, volleyball, soccer, and singles tennis also provide an aerobic workout. Participating in aerobic exercise at less than an aerobic level (below target heart rate) provides numerous health and fitness benefits, too, as part of maintaining a physically active lifestyle.

AEROBIC ACTIVITIES

basketball	bicycling
climbing stairs	cross-country running
cross-country skiing	dancing
handball	ice skating
inline skating	jogging
jumping rope	racquetball
roller skating	rowing
running	snow shoeing
soccer	spinning
stair-stepping	stationary cycling
swimming	tennis (singles)
volleyball	walking

See also CARDIAC CAPACITY; EXERCISE AND HEALTH; FLEXIBILITY; LIFESTYLE AND HEALTH; OBESITY AND HEALTH; RESISTANCE EXERCISE; STRENGTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

aging, changes in physical ability and fitness needs that occur with As a person grows older, his or her physical capabilities, STRENGTH, FLEXIBILITY, AEROBIC CAPACITY, exercise needs, metabolic rate, body composition, and risk for injury change.

Children and Exercise

Children require physical activity for proper development and growth. BONE and MUSCLE development relies in part on the stimulation from resistance activities such as walking and running. Preschool-age children tend to be on the go constantly. However, many develop fairly sedentary habits by the time they reach school age, with activities such as watching television, using the

computer, and playing video games replacing physical activities. Numerous clinical research studies correlate such physical inactivity with the rise in childhood OBESITY AND HEALTH conditions such as type 2 DIABETES, HYPERLIPIDEMIA, and OSTEOARTHRITIS that typically do not appear until middle age or later.

Health experts recommend an hour a day of moderate physical activity for children and adolescents, though estimate 60 percent or more do not meet that recommendation. The health risks associated with physical inactivity not only carry into adulthood but appear to be more severe. Aerobic capacity—the body's ability to use oxygen efficiently—reaches its peak in the early 20s and then begins a gradual decline. Muscle mass and BONE DENSITY are also at their peak in the early 20s. Daily physical activity in late ADOLESCENCE appears capable of extending aerobic capacity and musculoskeletal strength well into adulthood.

Older Adults and Exercise

A physically active adult has an aerobic capacity, measured as $\dot{V}O_{2max}$, up to 25 percent greater than a person of comparable age who does not exercise. Such a difference becomes increasingly significant with advancing age. Between age 20 and age 40 aerobic capacity declines 8 to 12 percent. Between age 40 and age 70 aerobic capacity declines about 10 percent per decade. After age 70 aerobic capacity declines 20 percent per decade. When daily physical activity is an element of lifestyle throughout life, the decline in aerobic capacity significantly slows. A 70-year-old who has a moderate to good FITNESS LEVEL (exercises at or beyond the minimum PHYSICAL ACTIVITY RECOMMENDATIONS) has an aerobic capacity comparable to that of a person 10 to 20 years younger.

Such a difference correlates to lower HEART RATE, lower BLOOD PRESSURE, stronger muscles and bones, increased HORMONE sensitivity and endocrine response, smoother and more regular gastrointestinal function, and even greater elasticity to the SKIN. These factors lower the risk for numerous health conditions including HEART disease, HEART ATTACK, STROKE, OSTEOPOROSIS, hip FRACTURE, type 2 diabetes, OBESITY, SEXUAL DYSFUNCTION, and various forms of cancer. Though no clinical evidence as yet supports exercise as a panacea for aging, researchers have gone so far as to say that lifestyle factors such as daily exercise, nutritious EATING HABITS, and not smoking have the capability to eliminate 85 percent or more of acquired CARDIOVASCULAR DISEASE (CVD). As well, numerous studies affirm the beneficial effects of exercise toward preventing injury and supporting overall health.

Daily physical activity becomes more significant with advancing age also because the body naturally begins to change in ways that diminish LEAN MUSCLE MASS, muscle strength, JOINT flexibility, gastrointestinal function, and hormone sensitivity. Around age 50 hormonal shifts in both men and women result in loss of muscle tissue, with fat often replacing this loss, and bone density. After age 70 muscle strength, bone density, and aerobic capacity decline in men and women alike. In men these changes are less pronounced; in women particularly they can have catastrophic health consequences if not detected and treated. A woman's risks for heart disease and osteoporosis jump after MENOPAUSE, largely the consequence of the drop in ESTROGENS. The risk of hip fracture due to lost bone density rises in men and women alike after age 70. Though daily exercise cannot prevent such changes from occurring, it can mitigate their severity and help maintain good QUALITY OF LIFE.

Older people who have chronic or serious health conditions may have limited ability to participate in physical activities. Conditions such as HEART FAILURE and CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) may limit aerobic capacity, for example. Osteoarthritis and RHEUMATOID ARTHRITIS may restrict movement. Despite the limitations chronic health conditions may impose on physical activity, they also benefit from regular exercise however modest. A health professional such as a physical therapist, an exercise physiologist, or a physiatrist (physician who specializes in rehabilitation medicine) can help develop an appropriate physical activity regimen for a person who has a chronic or debilitating health condition.

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; DISABILITY AND EXERCISE; WEIGHT LOSS AND WEIGHT MANAGEMENT; YOGA.

blister prevention Methods to reduce irritation to SKIN surfaces from friction. The feet are the most common site of blisters acquired during

physical exercise. Athletic activities such as racquet sports, rowing, baseball, golfing, bicycling, and sailing expose the hands to friction and the risk for blisters. A BLISTER is the body's attempt to protect itself from friction-generated injury. Fluid accumulates between the layers of the skin, separating the layers and buffering damage to the underlying delicate tissues. The process stimulates the NERVE endings in the skin to send signals of PAIN to the BRAIN. Blister prevention techniques attempt to anticipate sites of excessive friction to cushion them from irritation.

The right footwear can prevent many blisters from developing on the feet. It is important to wear shoes or boots that fit properly and are appropriate for the activity. Shoes that are too loose allow the foot and toes to slide against the inside of the shoe or the shoe to slip up and down on the heel. Shoes that are too tight pinch the toes and trap moisture against the skin. Even the best-fitting shoes or boots may cause blisters if they are not right for the activity. Socks absorb moisture and establish a physical barrier between the foot and the shoe; double-layer socks are most effective for this purpose. Socks should fit snugly and smoothly against the foot, and like shoes or boots should be appropriate for the intended use. People whose feet sweat excessively (HYPERHIDROSIS) may want to consult a podiatrist or dermatologist for evaluation and treatment to reduce the amount of moisture their feet produce.

Adhesive bandages, blister pads, moleskin, and other products can provide additional protection for areas that are particularly vulnerable to blisters, such as the back of the heels, the toes, and any parts of the foot that rub against the shoe. Some people apply petroleum jelly or antibiotic ointment to "hot spots." Other people find dusting the feet with foot powder or cornstarch, or applying a dry lubricant, helps keep the feet dry and smooths their movement within the shoes.

Athletic gloves, appropriate for the activity and that fit properly, can similarly protect the hands from friction and moisture. It is important for the glove to fit without bunching or pinching, otherwise the glove itself will become the cause of blisters. Rings worn on the fingers, even with gloves, can contribute to blisters by allowing the skin to pinch against them.

A CALLUS (thickened pad of skin) will eventually form at a site that repeatedly blisters, the body's further attempt to protect itself. Once a callus forms the area is much less likely to blister. Working up to a level of activity, such as with running or walking, helps prepare the skin for the exposure it faces. Blisters are more likely to occur when engaging in new activities or at a significantly increased level (such as a competitive event) within a familiar activity.

See also CHAFING; FITNESS LEVEL; PHYSICAL ACTIVITY RECOMMENDATIONS; TINEA INFECTIONS; WALKING FOR FITNESS.

C

carbohydrate loading The practice of consuming excess quantities of carbohydrates, such as pasta and breads, for a period of time before an athletic or competitive event. The body converts the excess GLUCOSE that results into glycogen, the short-term storage form of glucose held primarily in the LIVER. During exercise when the levels of glucose in the BLOOD circulation drop, the body begins to convert glycogen back to glucose to replenish glucose blood levels. Because carbohydrate loading increases the amount of glycogen the body stores, the athlete can sustain a higher level of energy output for a longer period of time.

The most common approach to carbohydrate loading is to eat primarily carbohydrates for three days before the scheduled event and to reduce the training schedule during that time to allow the body to store, rather than draw from, glycogen. Many top amateur and professional athletes practice some variation of carbohydrate loading, which is most effective for ENDURANCE activities that last two hours or longer. Fitness and nutrition experts also recommend eating a meal that contains both carbohydrates and protein about two hours after intense exercise to help the body replenish the stores of glucose and amino acids it drew from during the physical activity.

See also DIET AND HEALTH; EATING HABITS; NUTRIENTS; NUTRITIONAL NEEDS.

chafing Irritation to the SKIN resulting from clothing and body parts that rub. The areas most vulnerable to chafing are the inner thighs, groin, inner arms and sides of the chest, and front of the chest (especially the nipples). Ill-fitting clothing in combination with moisture is generally the precipitating factor. It is important to wear clothing appropriate for the activity and in most circumstances for the clothing to be snug though not constrictive. High-wicking fabrics in combination with talcum powder and similar products to absorb moisture further reduce the likelihood of chafing. Body lubricants, which form a barrier between clothing and the skin, extend protection for distance activities such as running, hiking, climbing, and bicycling. A CONDITIONING program of steady progress toward fitness goals also helps prepare the body, increasing its resistance to irritation.

See also BLISTER PREVENTION; FITNESS LEVEL; PHYSICAL ACTIVITY RECOMMENDATIONS; WALKING FOR FITNESS.

charleyhorse A sudden, intensely painful MUSCLE contraction, sometimes called a muscle CRAMP. A charleyhorse most often affects the legs and feet and is typically a consequence of electrolyte imbalances, especially deficiencies in magnesium and potassium. A charleyhorse may occur during rest, especially during sleep. A charleyhorse that occurs during exercise often indicated inadequate HYDRATION. Stretching and massaging the affected muscle often relieves the contraction, allowing the muscle to relax. Some people experience relief with ice applied to the area while other people find heat more helpful. Sometimes a degree of discomfort continues for a short time after the cramp subsides. Stretching and WARMUP before beginning exercise help prevent charleyhorses.

See also SHIN SPLINTS; STINGER.

conditioning A planned and consistent effort to establish and maintain, through physical exercise, a FITNESS LEVEL that supports health. Conditioning requires repetitious physical activity that exerts the body for STRENGTH, FLEXIBILITY, and AEROBIC CAPACITY. Physical conditioning may be part of a rehabilitation program for people recovering from

serious injury or health condition such as STROKE or HEART ATTACK. Conditioning is also an important component of the lifestyle changes necessary for effective WEIGHT LOSS AND WEIGHT MANAGEMENT.

Building a Conditioning Plan

It is important to build a conditioning plan that starts at the current fitness level and moves in progressive increments toward the target fitness level. There are numerous methods for assessing a person's existing fitness level. Health experts advise a ROUTINE MEDICAL EXAMINATION before beginning a new physical conditioning effort when any of the following circumstances apply

- physically inactive for longer than a year
- over age 50
- BODY MASS INDEX (BMI) over 32
- existing health conditions such as heart disease, DIABETES, OSTEOARTHRITIS, OBESITY, lung disease, or other chronic disorders
- physical limitations or disabilities

The most effective conditioning results occur with an approach that is structured and systematic, with planned activities intended specifically for exercise such as walking, bicycling, light weightlifting, and YOGA. Many people are able to also integrate activities of conditioning into their daily routines, such as walking to work or school and taking the stairs instead of the elevator. People whose jobs are physically active often have the strength and flexibility to accommodate the demands of their job tasks though may lack an overall state of physical fitness. A qualified fitness instructor can conduct a baseline assessment of the person's fitness status and help develop a conditioning plan that integrates work activities with fitness activities. The appropriate clothing, equipment, and technique for specific physical activities help ensure maximum benefit from the activities as well as minimize the risk for injury.

Maintaining a Conditioning Plan

Conditioning is successful when it becomes an element of lifestyle and an aspect of daily routine that incorporates a variety of daily activities that not only improve strength, flexibility, and aerobic capacity but also are activities a person enjoys. These activities, in combination, maintain the fitness of the entire body. RESISTANCE EXERCISE helps maintain BONE DENSITY and BONE strength, which is particularly important for women who are past MENOPAUSE. Regular physical activity also benefits emotional and psychological well-being. Many people find the commitment to planned exercise allows them time for themselves that provides a calming break from the stresses and pressures of work and family. Many activities also provide opportunities for recreation and social interaction, such as walking clubs, yoga groups, organized bicycling rides, group hikes, volksmarch and other volkssports, and structured classes at a gym or fitness facility.

CALISTHENICS FALLEN FROM FAVOR

Health and fitness experts no longer recommend old-fashioned calisthenics—situps, pullups, and pushups—once the staple of physical fitness programs because the resistance involved is that of body weight, which allows no FLEXIBILITY for either building up to a competence level or increasing the challenge to the body after reaching a level of competence with the exercises. As well, these exercises as taught in the middle decades of the 20th century place undue and potentially harmful strain on the joints and the lower back.

When circumstances interrupt conditioning it is important to get back on track as soon as possible, approaching it as any other integral component of lifestyle. It helps to maintain a modified conditioning effort when possible, such as alternative activities when traveling on business or recreation. Fitness level begins to slip after a week without any exercise at all, though is quickly recoverable with return to the regular physical activities. It is important to reenter the conditioning plan at the current fitness level and work back to the target fitness level.

See also ATHLETIC INJURIES; EXERCISE AND HEALTH; PHYSICAL ACTIVITY RECOMMENDATIONS; TRAINING; WALKING FOR FITNESS; WEEKEND WARRIOR.

cross training The practice of alternating different kinds of exercise to provide a well-rounded

workout for the body that establishes and maintains a high overall FITNESS LEVEL. Cross-training exercise typically complements a person's primary athletic activity. Runners may cross train by engaging in swimming to work the upper body, for example, and bicycle one day a week to work different muscles from those that running works in the lower body. Many athletes alternate AEROBIC EXERCISE with RESISTANCE EXERCISE to improve STRENGTH, such as weightlifting, with stretching activities to improve FLEXIBILITY, such as YOGA. The alternation may occur in the form of two or more activities in a single session or alternating activities among different sessions. For example a runner may run one day, lift weights the next day, run the next day, and swim the next day. Cross training also helps reduce the risk for ATHLETIC INJURIES.

See also AEROBIC CAPACITY.

D–E

disability and exercise Regular exercise is important for health and well-being for everyone, and most people are able to participate in physical activities to some degree. Though chronic or debilitating health conditions may limit a person's physical abilities, it is possible to adapt many physical activities to accommodate individual needs. For example, 30 minutes of pushing oneself in a wheelchair is comparable to 30 minutes of walking. In other circumstances health conditions such as moderate to severe CARDIOVASCULAR DISEASE (CVD) may limit AEROBIC CAPACITY; conditions such as CEREBRAL PALSY and OSTEOARTHRITIS may restrict FLEXIBILITY and mobility.

Anyone who has a physical disability should consult with his or her doctor before beginning a new physical activity or exercise plan.

Physical therapists and exercise physiologists, particularly those who specialize in sports medicine, can help people who have disabilities develop effective CONDITIONING or TRAINING plans and modify physical activities to meet their fitness goals and interests. Such modifications may take the form of adaptations in technique or alterations in intensity or duration of activity. Individual circumstances also may require adaptive clothing, shoes, and equipment. Many communities and fitness facilities have special physical fitness programs, including team and competitive events, for people who have disabilities; such programs allow participation at levels that match individual capabilities and interests.

Strengthening and flexibility activities are important for maintaining as much function as possible. Such activities improve BLOOD flow, particularly to the extremities and the SKIN. They also maintain BONE DENSITY and JOINT range of motion, permitting the best mobility possible. Passive exercise (in which a therapist or caregiver guides the person's body gently through structured movements) benefits people who have severely restricted mobility or PARALYSIS such as due to STROKE or SPINAL CORD INJURY.

See also AEROBIC EXERCISE; FITNESS LEVEL; PHYSICAL ACTIVITY RECOMMENDATIONS; RESISTANCE EXERCISE; STRENGTH.

endurance The ability to persist in performing a physical activity. Endurance may refer to AEROBIC CAPACITY (the fitness of the cardiovascular system), the ability to sustain a position over time (such as in YOGA), or the ability to repeatedly and consistently perform a set of movements (such as lifting weights). Endurance is an important element of overall physical fitness that requires an integration of aerobic capacity with STRENGTH and FLEXIBILITY.

Endurance improves with exercise that challenges the body's capabilities at a moderate level, encouraging the muscles to draw energy from glycogen stores and the LUNGS to function at higher efficiency in the amount of air, and consequently oxygen, they take in with each breath. Endurance training emphasizes activities that extend the duration of performance. For aerobic activities this means extending the length of time for TRAINING sessions in incremental fashion, for example increasing distance for running or the duration of holding a yoga pose. RESISTANCE EXERCISE also can improve endurance by increasing the number of repetitions of a resistance activity such as lifting weights or working with resistance bands.

See also CONDITIONING; FITNESS LEVEL.

exercise and health The correlations between daily physical exercise and health are numerous and solidly affirmed through clinical research studies. In an overarching context physical activity improves the efficiency of metabolic functions at the cellular level throughout the body. Physical exercise further has specific effects on nearly every system of the body, helping the body function with optimum efficiency.

Though researchers do not fully understand the mechanisms within the body through which exercise affects health and disease, they do know that physically inactive people are

- twice as likely to develop CORONARY ARTERY DISEASE (CAD)
- 50 percent more likely to develop HYPERTENSION (high BLOOD PRESSURE)
- up to 6 times more likely to develop type 2 DIABETES between the ages of 18 and 30
- twice as likely to die prematurely for any reason

Many researchers believe that physical inactivity is nearly as significant a risk factor for CARDIOVASCULAR DISEASE (CVD) as cigarette smoking. As well, the correlation between physical inactivity and OBESITY, also a key risk factor for numerous health conditions and premature death, is strong. Though in combination these two risk factors—physical inactivity and obesity—affect every level of bodily function from molecular (metabolic activity) to mechanical (how the body as a whole moves and performs) and are sometimes difficult to separate, exercise alone influences health in distinct ways. People who are overweight yet physically active every day have overall better health and lower risk for serious health conditions such as CVD and type 2 diabetes than people of comparable weight and are physically inactive. Very modest physical activity, such as walking 20 to 30 minutes every day, can result in significant weight loss over time, lowering health risk related to both obesity and physical inactivity.

Evidence conclusively demonstrates that regular exercise, done at least at the minimum level of recommended physical activity

- lowers BLOOD pressure and can reduce hypertension, decreasing the risk for STROKE
- improves INSULIN sensitivity, decreasing the risk for type 2 diabetes and helping stabilize diabetes that already exists
- reduces the risk for COLORECTAL CANCER, BREAST CANCER, and PROSTATE CANCER
- strengthens bones and increases BONE DENSITY, lowering the risk for OSTEOPOROSIS
- increases FLEXIBILITY and STRENGTH, improving mobility and reducing the risks for OSTEOARTHRITIS and injury from falls
- relieves stress and DEPRESSION, improving well-being and the ability to cope with daily difficulties and challenges
- lowers total CHOLESTEROL BLOOD LEVELS and increases high-density lipoprotein (HDL) cholesterol ("good" cholesterol) blood level, reducing the risk for ATHEROSCLEROSIS and CAD
- improves cardiovascular efficiency and lung capacity
- stimulates gastrointestinal activity, shortening the amount of time food takes to complete its journey through the digestive process and decreasing the likelihood of CONSTIPATION and other gastrointestinal disorders

Numerous studies show that modest to moderate physical exercise—30 minutes a day most days of the week—is sufficient to generate measurable health benefits. About 40 percent of Americans meet this objective. Additional exercise increases benefits. It is important to choose a variety of activities that are enjoyable, convenient (logistically feasible and require minimal preparation), within an individual's skill range, and safe within the context of any existing health conditions. Structured activities—even when structure is as basic as setting aside 30 minutes each day to walk—helps give exercise a sense of priority in a person's life, which encourages ongoing participation. Nevertheless, all efforts to increase physical activity in daily living, however small or brief, improve health and QUALITY OF LIFE. Consistency maintains fitness most effectively.

See also CHOLESTEROL, ENDOGENOUS; DIET AND HEALTH; EATING HABITS; HEALTH RISK FACTORS; LIFESTYLE AND HEALTH; METABOLISM; NUTRITIONAL NEEDS; OBESITY; OBESITY AND HEALTH; PHYSICAL ACTIVITY RECOMMENDATIONS; SMOKING CESSATION.

F

fitness level The ability of the body to perform physical activity. Fitness encompasses AEROBIC CAPACITY (cardiovascular fitness), STRENGTH, and FLEXIBILITY. These three components combine to help configure a person's LEAN MUSCLE MASS, BODY FAT PERCENTAGE, and BODY MASS INDEX (BMI), which are key risk factors for numerous health conditions, including CARDIOVASCULAR DISEASE (CVD) and DIABETES. A high fitness level, indicating daily physical exercise, reduces numerous HEALTH RISK FACTORS. Conversely a low fitness level, indicating physical inactivity, correlates to increased health risk.

Exercise physiologists use various scales to quantify an individual's fitness level. Some assessment scales emphasize cardiovascular fitness and others measure general fitness. CONDITIONING, which targets overall fitness status, and TRAINING, which prepares a person for a particular event or activity often at a competitive level, are structured methods to improve a person's fitness level.

People whose fitness levels are "very poor" or "poor" do not receive enough physical activity to support their bodies in health and are at increased risk for injury and health disorders. A "moderate" fitness level meets general PHYSICAL ACTIVITY RECOMMENDATIONS to support health, weight management, and reduction of health risk factors. People who have a "good" fitness level enjoy optimum benefit from physical activity. People who have a "very good" fitness level dedicate focused effort to physical fitness and are often athletes who participate in organized or competitive events.

As with EATING HABITS and nutrition, fitness level represents an integration of physical exercise into lifestyle such that activity is an inherent component of daily living. Many people can find ways to increase physical exercise through their daily activities, which can be as effective as structured exercise and makes the most of available time. Activities such as gardening, cleaning house, washing the car, mowing the grass (especially with a nonmotorized mower), and walking whenever possible are among the many ways to increase physical exertion on a daily basis that result in improved fitness level over time. Though physical activity recommendations and fitness level classifications may appear daunting to people who are not presently active and whose lives are busy, fitness is the accumulated result of numerous and daily small physical efforts that pay off in big ways when it comes to health as well as satisfaction with how one feels and looks.

See also BODY SHAPE AND CARDIOVASCULAR DISEASE; EXERCISE AND HEALTH; LIFESTYLE AND HEALTH; OBESITY; OBESITY AND HEALTH; WALKING FOR FITNESS; WEEKEND WARRIOR; WEIGHT LOSS AND WEIGHT MANAGEMENT.

flat feet A structural circumstance in which the ligaments in the foot do not support the bones to form an appreciable arch. The arch of the foot helps cushion the foot's structure during impact. Young children normally have flat feet until regular walking and running strengthens the muscles and ligaments of the feet, a process that typically occurs between the ages of 3 and 10 years. Unless there is an underlying deformity, there is no medical reason to attempt to treat flat feet in young children because it is the normal state of the feet.

Adults sometimes speak of having "fallen arches," a casual term that refers to stretching and loosening of the foot ligaments that sometimes occurs with increasing age. Flat feet that develop in such a way are more common in people who are physically inactive and overweight. Extra body weight stresses the feet's structure in the absence

GENERAL FITNESS LEVEL CLASSIFICATIONS

Fitness Level	Activities	Duration	Frequency
very poor	very little physical activity beyond that required for daily living (sedentary)	brief	seldom
poor	may walk at work, to and from the mailbox, and for tasks such as grocery shopping	one to two hours combined each day done	one to three days a week
moderate	walks one or two blocks at a time walks up two flights of stairs without shortness of breath some regular physical activity required at work (such as lifting or walking)	two to three hours combined each day done	three to five days a week
	YOGA, TAI CHI, or structured stretching exercises	10 to 20 minutes each day done	one to three days a week
	walk or casual bicycle ride for pleasure	20 to 30 minutes each day done	one to two days a week
good	walks for or more blocks at a time walks up three or more flights of stairs without shortness of breath job requires moderate physical activity	three or more hours combined each day done	four to five days a week
	participates in structured exercise activity	30 to 60 minutes combined each day done	three to five days a week
	yoga, tai chi, or structured stretching exercises	10 to 20 minutes combined each day done	three days a week
	lifts weights or works out with resistance bands	30 to 45 minutes combined each day done	three days a week
	brisk walk, moderate bicycle ride, run, or swim	30 to 90 minutes combined each day done	two to three days a week
very good	walks distances greater than ½ mile with ease walks up multiple flights of stairs without shortness of breath	one to three hours combined each day done	six or seven days a week
	lifts weights or works out with resistance bands	30 to 45 minutes combined each day done	three days a week
	job requires steady, moderate to vigorous physical activity	six to eight hours combined each day done	three to five days a week
	yoga, tai chi, or structured stretching exercises	10 to 30 minutes combined each day done	three to five days a week
	engages in moderate to vigorous aerobic activities or participates in competitive events	two to three hours combined each day done	two to five days a week

of physical exercise that would strengthen the muscles and ligaments.

Many adults who have flat feet have no discomfort or other symptoms and do not need treatment. Flat feet become problematic only when they cause abnormal pronation (side to side movement of the foot with impact), which can alter the alignment of the leg and thus affect the ankles, knees, and hips. For flat feet that cause discomfort, treatment is a combination of properly designed and fitted shoes along with shoe orthotics that support the inner surface of the arch area and the heel, stabilizing the foot during movement. Foot care experts typically further recommend a structured approach of planned, progressive physical activity to strengthen the structures of the foot as a component of an overall WEIGHT LOSS AND WEIGHT MANAGEMENT strategy. Rarely, flat feet may require surgery to tighten ligaments and realign the bones.

See also CONDITIONING; LIGAMENT; MUSCLE; OBESITY AND HEALTH; STRENGTH; SURGERY BENEFIT AND RISK ASSESSMENT; TALIPEDES.

flexibility The ease with which MUSCLE groups and joints allow movement. Flexibility is an integral though often undervalued component of overall physical fitness.

Fitness experts advocate stretching and WARMUP before and after physical activity, even that which is work related, to prepare the body for activity and reduce the risk for injury. Lack of use, injury, surgery, and health conditions such as OSTEOARTHRITIS may limit range of motion (the ability of a JOINT to move through the full scope of its capability). Exercises that improve range of motion include stretches and movements that prepare the joints for physical activity. YOGA, TAI CHI, and qigong also improve flexibility. Flexibility extends the ability of the body to participate in and benefit from strengthening and AEROBIC EXERCISE. Cycling and swimming combine the benefits of flexibility, strengh, and aerobic workouts.

See also AGING, CHANGES IN PHYSICAL ABILITY AND FITNESS NEEDS THAT OCCUR WITH; AEROBIC CAPACITY; ATHLETIC INJURIES; CONDITIONING; ENDURANCE; FITNESS LEVEL; STRENGTH; TRAINING; WEEKEND WARRIOR.

M

metabolic equivalent (MET) A unit of measure for the amount of oxygen the body uses during physical activity. One MET is equivalent to the oxygen an adult requires when sitting quietly for one minute. A four-MET activity, such as brisk walking or riding a bicycle on a level surface, requires four times the amount of energy (oxygen consumption) as the one-MET activity of sitting quietly. An eight-MET activity, such as running or riding a bicycle uphill, requires eight times as much energy as sitting quietly. METs are the basis for calculating the number of calories that particular activities burn. Activities that require three to six METs are considered to be of moderate intensity and burn 3.5 to 7 calories per minute. Activities that require greater than six METs are considered to be of vigorous intensity and burn more than 7 calories per minute.

Knowing an activity's MET value helps an individual calculate how long to participate in that activity to meet a desired level of CALORIE consumption. For example, a person who wants to burn 150 calories a day (the minimum recommendation for adults) may choose to walk at three and half miles per hour, a four-MET activity, for 40 minutes or run at five miles per hour, an eight-MET activity, for 20 minutes, depending on the desired level of intensity.

See also AEROBIC CAPACITY; AEROBIC EXERCISE; BODY MASS INDEX (BMI); CONDITIONING; FITNESS LEVEL; PHYSICAL EXERCISE RECOMMENDATIONS; TRAINING; WALKING FOR FITNESS.

metabolism The processes through which cells convert NUTRIENTS to energy. In the most basic sense, metabolism is the point of transition from energy intake (food consumption) to energy expenditure (molecular conversion). Multiple mechanisms within the body regulate the complex chemical interactions that constitute metabolism, with the HYPOTHALAMUS and the endocrine system taking the lead roles. Hormones such as THYROXIN (T_4), which the THYROID GLAND produces, and INSULIN, which the ISLETS OF LANGERHANS in the PANCREAS produce, determine the rate at which cells convert GLUCOSE (one of two fuel sources for cells) to energy. The hormones of the body's stress response—CORTISOL, EPINEPHRINE, and NOREPINEPHRINE—also can accelerate metabolism, usually as a short burst; though in times of trauma the STRESS RESPONSE HORMONAL CASCADE can alter the body's metabolism on a long-term basis as a mechanism to facilitate HEALING.

The common perception of metabolism is as a rate that represents a balance between calories consumed and calories expended. Metabolism may also refer to the processes that occur during digestion to convert foods and drugs into chemical molecules the body can use. Metabolism has two primary modes: anabolism and catabolism. Anabolism is energy expended toward construction (building tissue) and catabolism is energy expended toward destruction (breaking down tissue). Energy needs increase when a person is recovering from major surgery, injury, or illness, as the processes of healing engage the body in extra anabolic (constructive) effort.

Measuring Metabolic Rate

The fundamental measure of metabolism is the basal metabolic rate (BMR), which identifies the amount of energy, in terms of calories, that the body requires over 24 hours to function at absolute rest. Nutritionists and exercise physiologists generally use mathematical formulas to calculate BMR because its actual measurement is

complex and requires an overnight stay in a special lab to capture measurements at precisely the point of minimal metabolic activity. A common formula for estimating BMR is the Harris-Benedict equation. There are separate equations for women and for men, accommodating gender differences in the ratio of LEAN MUSCLE MASS to body fat.

Easier to measure directly is the resting metabolic rate (RMR), which provides similar information about the body's energy requirements at minimal activity. Many exercise physiology clinics can measure RMR. More sophisticated methods are available that allow determination of precise metabolic measures for elite athletes as well as for people who have severe health conditions. Most people expend 50 to 75 calories per hour at rest, so a rough generalization of metabolic rate is 1,200 to 1,800 calories. The larger a person, the higher his or her metabolic rate, whether body size results from MUSCLE mass or fat accumulation. However, increased muscle mass further raises the metabolic rate because muscle cells use more energy than fat cells in the normal course of their functions. Men generally have higher metabolic rates than women because their bodies have larger muscles and greater lean muscle mass.

Metabolism and Weight Management

From a practical perspective either RMR or BMR presents the body's energy needs in terms of calories, allowing an individual to estimate daily energy use (CALORIE expenditure) to tailor daily calorie intake. Activity factors and injury factors further determine the body's overall energy expenditure and intake needs. A person whose lifestyle is sedentary, for example, uses less energy and consequently requires less intake than a person whose lifestyle includes daily physical exercise. However, the metabolic rate decreases at about 5 percent per decade between the ages of 25 and 75, largely because lean muscle mass decrease; thus at age 75 a person requires about a third fewer calories each day than at age 25. Without a comparable increase in exercise, the difference can amount to a weight gain of four to seven pounds a year. Regular physical activity boosts the metabolic rate by maintaining a higher percentage of lean muscle mass.

Metabolic Response to Trauma

When the body experiences significant physical trauma, such as due to BURNS or major injuries, its natural stress response initiates metabolic changes that allow the body to rapidly convert protein to amino acids (and subsequently to glucose) for the body to use as energy. Major surgery may also initiate this response. The purpose of the metabolic response to trauma is to muster every available resource for healing; the result is rapid destruction (catabolism) of muscle tissue. During healing the metabolic rate rises significantly, reflecting the body's efforts to repair and reconstruct damaged tissue (anabolism). However, the rate of catabolism may be up to 10 times that of anabolism, establishing an imbalance that makes it difficult for the body to replace its protein stores.

Intensified nutritional support in combination with physical exercise (particularly RESISTANCE EXERCISE) can expedite muscle tissue restoration and help metabolism return back to normal. The most effective nutritional support incorporates a high-protein diet (up to two times the recommended dietary allowance) and NUTRITIONAL SUPPLEMENTS to supply increased amounts of certain B vitamins that are essential for cellular energy production and the efficiency with which cells can use glucose. Physical activity stimulates muscle cells to improve the efficiency with which they contract and relax, and encourages development of new muscle tissue. Sometimes doctors may prescribe hormones to further stimulate muscle growth.

Metabolic Disorders

Metabolic disorders are health conditions that alter the function of the body's metabolic, or energy-producing, pathways. Among the most common metabolic disorders are DIABETES, HYPERTHYROIDISM, HYPOTHYROIDISM, and PHENYLKETONURIA (PKU). Though doctors understand the mechanisms of most metabolic disorders, the causes remain largely unknown. Genetic factors play a significant role and may be the sole cause of certain metabolic conditions such as glycogen-storage disorders (which affect the body's ability to metabolize carbohydrates) and lipid-storage disorders (which affect the body's ability to metabolize fats).

Doctors commonly refer to genetic-based conditions as inborn errors of metabolism. Many of these disorders affect the function of specific enzymes that facilitate the conversion or storage of nutrients to energy within the metabolic pathway. The consequence may affect the body as a whole or the activity of specific kinds of cells such as muscle cells or nerve cells (neurons). Researchers do not know the extent to which genetic factors influence acquired metabolic conditions such as hyperthyroidism, hypothyroidism, and type 2 diabetes.

Symptoms of metabolic disorders vary depending on how the disorder affects metabolism and may include

- neurologic deficit and development delays
- CARDIOMYOPATHY
- hearing loss
- vision disturbances
- myoclonus
- seizures
- weakness or movement difficulties
- failure to thrive

Inborn disorders of metabolism may not become apparent until a child is several months to several years old, by which time the condition often causes significant damage to organ systems. Newborn screening for some such disorders, such as PKU, is common in the United States and many other countries. Early detection of PKU and many other metabolic disorders allows treatment or management, such as enzyme replacement therapy or dietary restrictions, to prevent the condition from causing damage. However, most genetic disorders of metabolism are not curable at present. Hormone replacement therapy is the treatment for hypothyroidism and insulin-dependent diabetes.

Confirming the diagnosis of metabolic disorders may be as simple as common blood tests, such as for diabetes or hypothyroidism, or may require sophisticated laboratory procedures and genetic (DNA) testing. There are no known methods of prevention for most metabolic conditions. Lifestyle factors such as diet and daily exercise can influence, and often prevent or reduce the severity of, type 2 diabetes.

DISORDERS OF METABOLISM

acid lipase disease	coenzyme A deficiencies
DIABETES	Fabry disease
G6PD DEFICIENCY	galactosemia
gangliosidoses	Gaucher disease
HEMOCHROMATOSIS	hyperoxaluria
HYPERTHYROIDISM	HYPOTHYROIDISM
lipidoses	metachromatic leukodystrophy
mitochondrial myopathies	muscular dystrophies
Niemann-Pick disease	OBESITY
oxalosis	PHENYLKETONURIA (PKU)
Tay-Sachs disease	WILSON'S DISEASE

Continuing advances in genetic and molecular research are allowing scientists to identify gene mutations that underlie a number previously poorly understood syndromes with symptoms of impaired physical and intellectual development. Researchers are hopeful that new findings will result in GENE THERAPY approaches to remedy or prevent the defective metabolic functions.

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; CELL STRUCTURE AND FUNCTION; EXERCISE AND HEALTH; HORMONE; METABOLIC EQUIVALENT (MET); NUTRITIONAL NEEDS; VITAMINS AND HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

P–R

physical activity recommendations The guidelines health and fitness experts suggest as minimum standards to maintain a FITNESS LEVEL that supports good health and reduces HEALTH RISK FACTORS for conditions such as CARDIOVASCULAR DISEASE (CVD), type 2 DIABETES, OSTEOPOROSIS, OSTEOARTHRITIS, and OBESITY. General physical activity recommendations emphasize AEROBIC EXERCISE to improve AEROBIC CAPACITY because this is the foundation for physical fitness.

The amount of physical activity necessary to have a positive effect on health is less than people commonly perceive. Recent research findings demonstrate that when it comes to exercise, a little goes a long way. Though more is nearly always better, the baseline recommendations for physical activity to support health are modest. To achieve and maintain a moderate fitness level health experts recommend healthy adults engage in

- 30 minutes of moderately intense physical activity on five days of each week

  and

- 20 minutes of vigorous physical activity on three days of each week

WARMUP and stretching should open and close every activity session, improving FLEXIBILITY and lowering the risk for injury. Walking is an ideal activity for exercise of moderate intensity and has the added advantage of being easy for most people to incorporate into their daily lifestyle routines. Walking is also a good RESISTANCE EXERCISE, improving BONE DENSITY. Short sessions, such as 5 to 10 minutes at a time, that add up to 30 minutes over the course of a day are as effective as a single, continuous 30-minute sessions.

Vigorous physical activities are those which raise HEART RATE to 60 percent of maximum for 20 minutes or longer and consume 7 calories or more (eight metabolic equivalents [METs]) per minute. Running, bicycling, swimming, cross-country skiing, jumping rope, step aerobics, aerobic dance, rowing, and stair stepping are among the numerous activities capable of accomplishing this objective. Vigorous physical exercise is most effective when it continues for 20 minutes or longer. Most vigorous exercise also incorporates resistance, increasing MUSCLE STRENGTH and mass as well as supporting BONE density.

Meeting these recommendations increases energy expenditure by 1,200 to 1,400 calories each week, helping with WEIGHT LOSS AND WEIGHT MANAGEMENT. For a person striving to lose weight, exercising at the recommended level can allow weight loss of 18 to 21 pounds over the course of a year without a change in the number of calories consumed. Exercise in combination with nutritious EATING HABITS that maintain dietary intake at the recommended level further expedites weight loss. Adding physical activity beyond these recommendations, which health experts encourage, further improves physical fitness and aerobic capacity and lowers health risk factors for HYPERTENSION (high BLOOD PRESSURE), HYPERLIPIDEMIA, ATHEROSCLEROSIS, CORONARY ARTERY DISEASE (CAD), and INSULIN RESISTANCE.

Health experts recommend a minimum of 60 minutes of moderate physical activity daily (seven days a week) for children and adolescents. Research findings support the belief that such a level of physical activity provides health benefits that extend well into adulthood. Among these benefits are strong bones, cardiovascular effi-

ciency, flexible joints, and healthy BODY MASS INDEX (BMI). Regular physical activity during childhood appears to further reduce risk factors for numerous health conditions in adulthood, even when activity eases. Children for whom daily exercise is a part of lifestyle are far more inclined to maintain physical activity as a priority in adulthood.

See also EXERCISE AND HEALTH; HEALTHY PEOPLE 2010; METABOLIC EQUIVALENT (MET); NUTRITIONAL NEEDS; WALKING FOR FITNESS.

protein loading The practice of consuming increased quantities of protein, such as in meats, for a period of time before an athletic event. Some athletes who participate in activities that require MUSCLE STRENGTH eat high amounts of protein to help build muscle mass. Though the body requires amino acids, which it acquires from dietary proteins, to repair and maintain tissues of all kinds throughout the body, including muscle tissue, a typical diet that contains about 15 percent protein generally meets the body's protein needs.

Excessive quantities of protein consumed in the diet, like excesses of dietary fats and carbohydrates, eventually becomes first GLUCOSE and then glycogen (short-term energy storage) and fat (long-term energy storage). Some studies suggest that long-term excessive protein consumption (usually of protein supplements) can strain the filtering mechanism of the KIDNEYS and can cause kidney damage. However, these findings are inconclusive, particularly in people who have normal kidney function and have no significant health conditions.

Nutrition and fitness experts recommend eating a meal that contains primarily carbohydrates and protein about two hours after intense exercise or a competitive event to help the body more quickly replenish the stores of glucose and amino acids it drew on during the physical activity. Most health experts do not recommend protein loading before an event or a competition, and recommend protein supplements only for people who cannot obtain adequate dietary protein because of health conditions.

See also CARBOHYDRATE LOADING; DIET AND HEALTH; NUTRIENTS; NUTRITIONAL NEEDS; NUTRITIONAL SUPPLEMENTS.

resistance exercise Physical activity, also called resistance TRAINING, in which the muscles exert effort against pressure, such as lifting weights. Resistance exercise, often called weight training when it involves the use of weights, enlarges and strengthens muscles and decreases body fat. It also improves the ability of the bones to retain calcium, maintaining BONE DENSITY and STRENGTH. Resistance exercise is particularly important for women over the age of 50, as BONE loss that can lead to OSTEOPOROSIS becomes a significant concern after MENOPAUSE. Health and fitness experts recommend resistance exercise two or three days a week, alternating with AEROBIC EXERCISE for a comprehensive fitness program.

BIG MUSCLES

Some people desire and other people dread the prospect of bulky muscles. Conventional resistance exercise is more likely to disappoint the former and please the latter. Though resistance exercise decreases the number of fat cells in MUSCLE tissue to give the muscles firmness and definition, it does not generate monster muscles.

A methodical approach exercise physiologists call progressive overload is the key to effective resistance training. Progressive overload is the practice of periodically increasing the difficulty of resistance as MUSCLE groups develop strength and become accustomed to the established resistance level. Most people should increase resistance every six to eight resistance exercise sessions, or about every two weeks. When working with weights, progressive overload can take place by increasing the amount of weight (intensity), the number of repetitions (duration), or the number of sessions (frequency). Many people combine these approaches. Resistance bands, another popular method of resistance exercise, come in different resistance levels, though generally the same concepts of progressive overload apply.

Each resistance exercise session should include multiple sets with rest periods of one to two minutes between each set. Rest, which allows the muscles to recover and "learn" the exercise (muscle memory), is a crucial component of a resistance exercise program. For most people, 20 to 40

minutes of resistance exercise is sufficient. Athletes in training for events or a competitive season may engage in longer sessions. Some people move from one muscle group to the next within each session; other people focus on one muscle group in each session, working a different muscle group the next session.

Resistance exercise also encompasses activities that exert pressure against the musculoskeletal system, such as walking and running, which some people refer to as impact exercise. Nonimpact activities such as moderate to intense bicycling and cross-country skiing challenge the musculoskeletal system in the same fashion as working out with weights. These activities further build strength and increase FLEXIBILITY.

RESISTANCE ACTIVITIES	
body bar	free weights
pullups	pushups
resistance bands	running
walking	weight machine

See also AEROBIC CAPACITY; ENDURANCE; FITNESS LEVEL; HEALTHY PEOPLE 2010; PHYSICAL ACTIVITY RECOMMENDATIONS.

S–T

shin splints PAIN along the tibia, the area in the lower leg commonly called the shin. Shin splints are common among people who participate in physical activities such as walking, running, marching, and hiking. Pain is the primary symptom, often occurring at the start of the activity, subsiding as the activity continues, and returning up to several hours after the activity ends. The affected area of the leg is tender to the touch.

Simple shin splints seldom require a doctor's attention; treatment is rest. Many people find ice, applied two or three times a day for 20 minutes eases the pain. NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) can relieve INFLAMMATION. Full HEALING takes three to four weeks; it is important to avoid the responsible activity during this time. Substituting nonimpact activities, such as bicycling and swimming, can help maintain FITNESS LEVEL or continue a training regimen during the healing period.

Because the pain of shin splints can be intense, people often worry about stress FRACTURE. Stress fracture is much less common than shin splints and occurs with extensive, repeated trauma over time or when TRAINING for an event bumps up the level of intensity, whereas shin splints is a soft tissue injury that typically occurs when starting a new activity after a period of inactivity.

Properly fitted footwear appropriate for the activity in combination with proper technique can reduce the risk for shin splints and other repetitive trauma injuries. Some people benefit from shoe orthotics, devices that correct pronation (the angle of the foot on impact). However, hard surfaces such as pavement and concrete challenge even the best footwear and technique. Rest from the activity at the first signs of shin splints can avert extended down time.

See also ATHLETIC INJURIES; CONDITIONING; FLAT FEET; SPRAINS AND STRAINS.

sports drinks and foods Specialty products marketed as beneficial for replenishing NUTRIENTS during and after exercise. Though many people use these products, most do not need or derive much benefit from them. Health and fitness experts recommend following nutritious EATING HABITS to maintain the body's level of nutrients at optimal level and maintaining adequate HYDRATION by drinking sufficient water before, during, and after exercise. Sports products are most helpful for people who exercise at high intensity for extended periods of time, such as those who participate in competitive ENDURANCE events such as randonneuring, climbing, triathlon, or marathon. In such circumstances, using these products to supplement nutritional needs can provide a steady source of energy to fuel the body's intensified activity.

Products and nutritional supplements that contain ephedra (which is banned in the United States) or the Chinese herb ma huang, which are STIMULANTS, may cause dangerous ARRHYTHMIA (irregularity of the HEART RATE).

Many energy and sports drink products contain high amounts of sugars, which can deliver an energy boost in the form of simple carbohydrates. They also deliver significant calories. Some products also contain CAFFEINE or herbal STIMULANTS such as GINSENG. Sports and nutrition bars may be primarily carbohydrates as well, though some products contain a mix of carbohydrates, proteins, and fats that can provide quick nutrition when

eating other foods is impractical. It is important to read product labels carefully.

See also DIET AND HEALTH.

stinger An injury to the brachial plexus, the large NERVE cluster that branches from the SPINAL CORD to innervate the shoulder, arm, and hand.

An injury that causes numbness on both sides of the body suggests SPINAL CORD damage and requires immediate medical attention. Only medical personnel should attempt to move a person who has a possible SPINAL CORD INJURY.

A stinger, also called a burner, is a common injury in contact sports and occurs when a blow or intense pressure displaces the neck and the compresses the cervical nerve roots between the cervical vertebrae (spinal bones in the neck). The compression causes symptoms that include sharp burning or stinging and numbness. Though the discomfort can be severe, it generally goes away within minutes. Occasionally symptoms may continue for up to several weeks. An isolated stinger leaves no residual damage, though repeated stingers can cause permanent damage to the nerves. The injury at the neck affects the shoulder and arm on the opposite (contralateral) side.

See also ATHLETIC INJURIES; NEURITIS; NEUROPATHY.

strength The ability of a MUSCLE to engage in physical activity, particularly resistance activity. Common measures of strength are the abilities to move weight (such as in weightlifting) or to exert force against pressure (such as in bicycling or rowing). Strength improves through repetitious actions that generate force against muscle fibers as they contract and relax, which causes them to enlarge as well as become more efficient in their use of oxygen. Muscles exposed to consistent exercise develop denser networks of capillaries, facilitating rapid oxygen exchange, and larger mitochondria capable of expanded functions. Mitochondria are the "engines" of the cell, performing multiple metabolic tasks that allow cells to generate and use energy. As muscles become stronger and larger, they require more challenge in the form of increased weight or resistance to maintain their strength.

PAIN is a signal that the body has reached its limit or is injured. Stop a strengthening activity at the first indication of pain. Rest five minutes and try the activity again. If the pain persists, stop the session and implement relief measures such as rest and ice to the area.

When exercising with weights it is important to start at an appropriate level for both the amount of weight and number of repetitions and work up to the desired level. Excessive weight can cause injury and inadequate weight does not challenge the muscles. In general, a person should be able to perform 8 repetitions with a particular weight, feeling some resistance though no PAIN with each repetition. When it becomes easy to do 12 to 15 repetitions, the muscle group is ready for an increase in weight. At the new weight, start again with 8 repetitions and increase as the repetitions become easier to perform. Fewer repetitions with heavier weight builds muscle mass and increases strength faster than more repetitions with lighter weight, though the latter builds ENDURANCE. Specific weight TRAINING regimens may have different guidelines.

The body itself can become the source of weight and resistance. Exercises such as curls, pushups, pullups, and squats use the body's weight to generate resistance against movement. The drawback to these exercises is that body weight is inflexible as the source of resistance; one cannot built up to or increase the effect.

Physical activities that use large muscle groups in repetitious activity also use the body's weight as resistance against gravity (such as with walking and running) or against equipment and gravity (such as with cycling and rowing). Aerobic activities such as swimming further tone muscles and improve AEROBIC CAPACITY though are not as effective for strengthening. A person can expect to see a 20 percent increase in strength after two months and a 40 percent increase in strength after four to six months of consistent strength training.

Many factors influence how strong muscles can become, key among them being regular participa-

tion in strengthening activities (such as RESISTANCE EXERCISE), FITNESS LEVEL, FLEXIBILITY, and the range of motion of the joints. Additional factors that may become important for competitive athletes include individual genetic characteristics and physical structure, which influence the manner and rate at which muscle fibers contract, relax, and recover. Rest is an important element of resistance exercise or strength training. Most regimens alter body regions, such as upper body one day and lower body the next day or rotate strengthening activities with endurance activities.

Strength exercises are particularly important for adults over age 65, helping sustain a high percentage of LEAN MUSCLE MASS as well as to maintain BONE DENSITY and BONE strength. Lean muscle mass naturally declines with advancing age, with fat cells replacing muscle cells. Activity that challenges the muscles encourages conversion of fat to muscle, improving lean muscle mass. Changes in HORMONE levels in the body, particularly in women after MENOPAUSE, cause changes in the amounts of calcium in the BLOOD circulation that regulate how much calcium enters and leaves the bones. Regular muscle activity improves calcium distribution mechanisms, keeping more calcium in the bones.

See also AEROBIC EXERCISE; CONDITIONING; DISABILITY AND EXERCISE; PHYSICAL ACTIVITY RECOMMENDATIONS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

training The process of improving the body's FITNESS LEVEL through targeted, repetitious physical activity that has specific goals. Training also may refer to the preparation necessary for an event such as a race or a circumstance such as a sports season. The premise of training is to gradually escalate the challenge to the muscles for improved STRENGTH and FLEXIBILITY and to increase AEROBIC CAPACITY for improved ENDURANCE.

Building a Training Regimen

A typical training regimen emphasizes preparation for the dominant activity, for example running or playing tennis. Flexibility, strength, and AEROBIC EXERCISE target measurable improvement in the activity's performance. A runner may strive for a faster pace, a tennis player may aim for a stronger serve or backhand. Short, focused sessions are most effective at the onset of a training regimen, with incremental increases in intensity and duration as ability and fitness improve. It is important to have specific, stepped goals and methods for measuring progress toward them. Goals should accommodate competitive as well as personal factors. A new runner might establish first level goals of achieving a 12-minute mile and completing a 5-K race or organized running event, for example. Proper nutrition and HYDRATION are essential as well.

Most people benefit from the advice of experts in their chosen activities, such as by taking classes, joining clubs, or researching training methods in books and on the Internet. Such advice can jumpstart a training regimen, getting to the core of methods with proven effectiveness as well as reducing the likelihood of injury. The most common injuries that occur early in a training regimen are those related to doing too much too fast or to inadequate WARMUP. Such injuries are generally preventable through proper technique and include MUSCLE soreness, blisters, CHAFING, and SPRAINS AND STRAINS.

TIPS FOR SUCCESSFUL PHYSICAL TRAINING

- When starting a training regimen, begin slowly and aim for steady improvement.
- Establish specific goals and methods for measuring progress toward them.
- Start and end every training session with WARMUP exercises and stretches.
- Vary activities to let the body recover, keep interest, and improve overall fitness.
- Increase intensity and duration in increments as ability and fitness improve.
- Eat nutritiously and drink water often.
- Enjoy the chosen activities.

Maintaining a Training Regimen

Once a person reaches his or her desired training level, it is important to continue varying activities and intensity levels to provide a mix of challenges for the body. Some people alternate types of activities each day, for example doing an aerobic activity one day and weight training or resistance training the next. Other people prefer to mix it up within each exercise session.

It is also important to let the body rest. Competitive athletes often incorporate "time off" from

their primary sports into their training regimens, using other activities to exercise their bodies in different ways. A runner or bicyclist may swim and jump rope for aerobic exercise, for example. Rest allows the body to heal any minor injuries as well as to recover its capacity to perform, particularly after participation in a competition or organized event.

Philosophies differ on the optimal approach to final preparation for a competitive or organized event. Many sports trainers recommend backing off on training for 5 days before the event, engaging in light activity to keep the body flexible but not at such a level as to exert the muscles or aerobic capacity. A bicyclist training for a century ride (100 miles), for example, may do an 85- to 100-mile ride 10 days before the event, ride 30 to 45 miles every other day until 5 days before the event, and not ride again until the event. A tennis player may engage in two-a-day sessions until the week before a match, drop to a couple days of light volley practice, and then rest until the match. The premise behind this approach is to let the body fully recover and prime itself at its optimal performance level; thus may also minimize the risk for injury. A competitive athlete may choose to consult or work with a personal trainer who can tailor specific training activities, including nutrition and hydration, for his or her individual needs.

Clothing, Equipment, and Technique

The proper clothing, equipment, and techniques are important for safety as well as performance in any training regimen. Every activity has specialized items that are either necessary or make the activity easier and safer to perform. Safety equipment, such as helmets and EYE protection, is crucial in many activities. The right clothing, such as padded bicycle shorts or walking shoes, cushions and protects the body. Proper technique is essential for improvement toward performance goals as well as to reduce the risk for injury. It is important to choose equipment and clothing that is appropriate for the activity and that fits the individual.

See also ATHLETIC INJURIES; PHYSICAL ACTIVITY RECOMMENDATIONS; RESISTANCE EXERCISE; WEEKEND WARRIOR.

W

walking for fitness A planned approach for improving and maintaining overall physical fitness and health through walking. Health and fitness experts believe walking is the ideal exercise for people of nearly any age, FITNESS LEVEL, and health status. Walking is also an excellent component of any WEIGHT LOSS AND WEIGHT MANAGEMENT strategy. Everyday walking is a good means for becoming consistently more active. Walking for fitness takes walking to the next level, integrating it into one's individual lifestyle as an activity in its own right. Though walking alone will allow most people to reach the minimum recommended level of physical activity, walking in combination with other physical activity such as lifting weights (RESISTANCE EXERCISE and STRENGTH exercise) and swimming or bicycling (moderate to vigorous AEROBIC EXERCISE) provides a more vigorous workout.

As with any physical activity, it is important to dress appropriately and plan a gradual progression of pace and time. Clothing should fit comfortably enough to allow free movement but not be baggy. Fabrics that wick moisture minimize CHAFING. Though 100 percent cotton is comfortable for casual wear, it is not a good fabric for exercise because it tends to absorb rather than wick away moisture. Wet clothing contributes to BLISTER formation, chafing, and chilling. There are technical fabrics on the market, available in casual as well as athletic styles, that pull perspiration away from the body to keep the SKIN surface dry. Shoes should be designed for walking and fit snugly without pinching or gapping. Double-layer walking socks absorb friction to help prevent blisters.

A person whose lifestyle is physically inactive may want to start with a relaxed pace of two miles per hour, walking for 5 to 15 minutes at a time. Health experts recommend minimum physical activity sufficient to use 150 calories each day (1,000 calories a week). Sustained periods of exercise that raise the HEART RATE and BREATHING rate for 20 minutes at a time or longer help develop AEROBIC CAPACITY. BODY MASS INDEX (BMI) influences the pace and time necessary to reach this goal. As well, varying the walking pace and time achieves this goal in different ways depending on a person's interests and circumstances (such as time constraints). A general guideline is to increase the intensity of exercise no greater than 10 percent per week. Pushing to reach a higher level of intensity increases the risk for injury.

The accompanying table shows the approximate energy output (number of calories burned) for different paces and times at representative BMIs for individuals at healthy weight (BMI range 18.5 to 24.9), at overweight (BMI range 25 to 29.9), and at OBESITY (BMI 30 and above). The higher one's BMI, the more calories required to perform the activity. The slower the pace, the more time walking necessary to meet the minimum recommended daily activity level for calories consumed in physical exercise. A pedometer, a computerized device that clips to a belt or the edge of a pocket, functions as a timer and counts strides to measure pace and distance. Many pedometer models also calculate calories consumed and average pace.

See also AGING, CHANGES IN PHYSICAL ABILITY AND FITNESS NEEDS THAT OCCUR WITH; BLISTER PREVENTION; CONDITIONING; DISABILITY AND EXERCISE; OSTEOPOROSIS; PHYSICAL ACTIVITY RECOMMENDATIONS; SHIN SPLINTS; WEEKEND WARRIOR.

warmup Stretches and light-intensity movements that prepare the muscles and joints for physical activity. Warmups increase BLOOD flow to

WALKING FOR FITNESS: APPROXIMATE ENERGY OUTPUT

Walking Pace	Walking Time	Walking Distance	Energy Used (Calories)		
			BMI 22 (healthy)	BMI 27 (overweight)	BMI 32 (obesity)
2 mph (relaxed)	15 minutes	½ mile	43.75	53.75	63.75
2 mph (relaxed)	30 minutes	1 mile	87.5	107.5	127.5
2 mph (relaxed)	45 minutes	1½ miles	131.25	161.25*	191.25*
2 mph (relaxed)	1 hour	2 miles	175*	215	255
3 mph (moderate)	15 minutes	¾ mile	57.5	70	83.75
3 mph (moderate)	30 minutes	1½ miles	115	140	167.5*
3 mph (moderate)	45 minutes	2¼ miles	172.5*	210*	251.5
3 mph (moderate)	1 hour	3 miles	230	280	335
4 mph (brisk)	15 minutes	1 mile	87.5	106.25	126.25
4 mph (brisk)	30 minutes	2 miles	175*	212.5*	252.5*
4 mph (brisk)	45 minutes	3 miles	262.5	318.75	378.75
4 mph (brisk)	1 hour	4 miles	350	425	505
5 mph (fast)	15 minutes	1¼ miles	137.5	170*	202.5*
5 mph (fast)	30 minutes	2½ miles	275*	340	405
5 mph (fast)	45 minutes	3¾ miles	412.5	510	607.5
5 mph (fast)	1 hour	5 miles	550	680	810

**Passes minimum daily physical activity recommendation*

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the muscles, bringing more oxygen and enhancing the ability of the BLOOD to carry away metabolic wastes, such as lactic acid, that result when MUSCLE cells contract. Fitness experts recommend 10 to 15 minutes of warmup before activity and 5 to 10 minutes of the same warmup routine after activity. Warmup stretches and movements after activity, sometimes called cool-down, ease the transition of the muscles back to a less intense level.

A general approach to a warmup is to begin with either the feet or the head and gently move and stretch each group of muscles, taking 5 to 7 minutes to cover the entire body. Then spend another 5 to 10 minutes slowly engaging in the planned activity, easing the muscles into the patterns of its movements and efforts. Some people run in place for a few minutes to loosen the muscles and joints. YOGA postures are effective for stretching and FLEXIBILITY. After the activity, repeat

the process in reverse. Spend about 5 minutes going slowly through the movements of the activity, then take 5 to 7 minutes to stretch and sequentially move the muscles in groups for the entire body.

See also CONDITIONING; FITNESS LEVEL; HYDRATION; TRAINING.

weak ankles A circumstance in which the ligaments and muscles of the ankles are lax, failing to provide the ankle with the stability it requires to support the body during physical exercise. Weak ankles often result from physical inactivity though may also occur after injury or surgery to the ankle. Excessive body weight exacerbates the situation. A weak ankle has a tendency to allow the foot to roll inward or outward, presenting risk for sprain (stretched LIGAMENT) or ACHILLES TENDON INJURY. A planned program of structured exercise to strengthen the ankle's ligaments and muscles, coupled with weight loss if indicated, improves weak ankles for most people. Properly fitted shoes that provide good support for the foot further improve the ankle's stability. Some people benefit from wrapping or taping the ankles before activity.

See also CONDITIONING; FLAT FEET; MUSCLE; PHYSICAL THERAPY; SPRAINS AND STRAINS; TENDON; WEIGHT LOSS AND WEIGHT MANAGEMENT.

weekend warrior An individual who participates in intense physical activities on the weekends but gets very little physical activity during the week. There is a tendency to make the most of available free time by doing as much activity as possible. The risk of injury, especially soft tissue injuries such as SPRAINS AND STRAINS, is much higher with this pattern of exercise. WARMUP is especially important to help relax and the muscles and prepare them for activity. Proper nutrition and HYDRATION before, during, and after exercise is essential.

Many people slip into weekend warrior patterns because they do not have time during the work week to participate in exercise activities at the same intensity level. However, even short periods of moderate exercise improve STRENGTH, FLEXIBILITY, and stamina to make weekend activities more enjoyable as well as reduce the risk for injury. People who participate in competitive events or strenuous physical activities on the weekends can bump up their level of daily activity by running stairs, lifting hand weights, and doing stretching and strengthening exercises. The greatest health benefits come from a pattern of regular activity. Health experts recommend daily walking at a minimum (30 to 45 minutes, five to seven days a week).

Some soreness and aches are reasonable to expect after a weekend of intense activity or a competitive event. Ice or heat often provide relief. However, most such discomforts should be gone within a day or two. Those that linger to the next weekend or that limit function may indicate an injury that a doctor should evaluate.

See also ATHLETIC INJURIES; CONDITIONING; EXERCISE AND HEALTH; PHYSICAL ACTIVITY RECOMMENDATIONS.

HUMAN RELATIONS

The area of human relations covers the interactions between people as those interactions affect overall health, specific health conditions, and QUALITY OF LIFE. *Practitioners who provide services within human relations may be psychologists, social workers, mental health nurse practitioners (MHNPs), professional counselors, school counselors, and organizational development specialists.*

This section, "Human Relations," presents an overview discussion of the general relationship between human interaction and health and entries about specific issues within human relations. The section "Psychiatric Disorders and Psychologic Conditions" presents entries about the health and health conditions of thought and emotion. The section "The Nervous System" contains content about the health and health conditions of the structures of the BRAIN and nerves.

Human Interactions and Health

The diagnostic models of many Eastern health systems evaluate an individual's temperament and overall circumstances in conjunction with, as well as on equal standing with, physical signs such as PULSE and body temperature. Interest in how people and their interactions with one another as well as with their environments entered the realm of Western medicine's empirical evidence model in the 1950s when research began to confirm correlations between factors such as stress and health conditions such as CARDIOVASCULAR DISEASE (CVD). Other associations rapidly emerged, quantifying and substantiating the complex relationships among health, disease, attitudes, and satisfaction with life circumstances.

Social relationships are crucial in the human experience, ranging from the limited though sometimes intense interactions of in the workplace to lifelong friendships to the emotionally and physically intimate partnerships of romantic partners to the bonds of family. Relationships are the framework of culture and society, around the world and across generations. They are essential to health and often play roles, directly and indirectly, in the development of disease.

Interventions to Treat or Prevent Disease

Awareness of the interactions between social relationships and health provides opportunity to prevent adverse effects. Stress is perhaps the classic example, as much research in recent decades has illuminated the numerous and varied effects of emotional and psychologic stress on physical health. Stress may arise from any aspect of human relations or social settings, from family to work, and may manifest through diverse expressions ranging from outwardly explosive anger or acts of VIOLENCE to inwardly ravaging disease processes such as CVD. Sustained emotional stress can maintain BLOOD PRESSURE and HEART RATE at higher than normal levels for extended periods of time, potentially altering the function of the cardiovascular system in negative and permanent ways. Recognizing and learning to manage the underlying factors responsible for such stress may mitigate the physiologic and health consequences.

At the other end of the spectrum is growing awareness of the extent to which a person's spiritual beliefs and cultural traditions affect the perceptions of health and disease as well as receptiveness to treatments. Health-care providers are quick to point out that despite the astonishing technologic advances of recent decades, much of modern medicine remains more art than science.

How people feel about themselves, their health situations, the partnerships and relationships in their lives, and their reasons for living may ultimately have greater significance in preventing and treating health conditions than medications, surgeries, and high-tech therapies.

A

adolescence The stage of emotional and mental development that marks the transition from childhood to adulthood, accompanying the physical transition that occurs with PUBERTY. By adolescence an individual has the physical appearance and characteristics of an adult, including sexual maturity and reproductive capability though does not yet have complete neurologic development and psychologic and emotional maturity.

Though most of the health issues of concern in adolescence may occur at any age, some may be difficult to distinguish from the normal turbulence of this developmental period. The risk for some health conditions is highest during adolescence, such as ACCIDENTAL INJURIES and SEXUALLY TRANSMITTED DISEASES (STDS), because adolescence represents a unique convergence of an intense desire to explore adult behaviors with an immature sense of consequences. During adolescence most Americans learn to drive, start dating, and begin working, all of which are important steps in the transition to independence and adult responsibilities yet expose young people to new risks.

Though the general age of consent (legal adulthood) is 18 in the United States (though 21 for ALCOHOL purchase and consumption), the age of consent for health-care services and medical treatment varies among states. Some states grant the right to receive health-care services and medical treatment for certain circumstances (such as mental health, CONTRACEPTION, PREGNANCY, and SEXUAL HEALTH) as early as age 14 though require the authorization of a parent or legal guardian for surgery, invasive diagnostic or therapeutic procedures, and most nonemergency health-care services until the child reaches age 18. Hospitals, health-care providers, and public health agencies know the limits and constraints of applicable laws and regulations, which are subject to change as a consequence of legislation (new laws) or legal rulings (court cases).

HEALTH CONCERNS COMMON IN ADOLESCENCE

ACCIDENTAL INJURIES	ACNE
ALCOHOL abuse	BODY DYSMORPHIC DISORDER
cigarette smoking	CONDUCT DISORDER
DEPRESSION	EATING DISORDERS
GENERAL ANXIETY DISORDER (GAD)	OBESITY
OBSESSIVE–COMPULSIVE DISORDER (OCD)	OPPOSITIONAL DEFIANT DISORDER
PEER PRESSURE	SEXUAL ASSAULT
SEXUAL HEALTH	SEXUALITY
SEXUALLY TRANSMITTED DISEASES (STDS)	substance abuse
trauma	SUICIDAL IDEATION AND SUICIDE
unintended PREGNANCY	VIOLENCE

See also PARENTING; PEER PRESSURE; SECONDARY SEXUAL CHARACTERISTICS; SEXUAL ORIENTATION; YOUTH HIGH-RISK BEHAVIOR.

anger and anger management Anger is a natural, intense emotion of displeasure that represents an interaction between the limbic system, which directs the body's emotional responses, and the frontal lobes of the cerebral cortex, which both interpret information and initiate conscious behavior in response. The frontal lobes are also the source of conscious inhibition, the innate mechanisms that control extremes in emotional expression and behavior. Anger's expression is normal and essential and may span the spectrum from irritation to rage.

Anger results in physiologic changes within the body. The STRESS RESPONSE HORMONAL CASCADE releases surges of CORTISOL, EPINEPHRINE, and NOREPI-

NEPHRINE—the stress hormones. This cascade causes BLOOD vessels throughout the body to constrict, raising BLOOD PRESSURE. It also causes HEART RATE to go up and BREATHING rate to increase. These changes can take place within seconds, though the body takes much longer to return to normal.

Anger can become a personal health issue or a social problem when its expression is inappropriate or when it is a persistent state of being. On the health front, prolonged elevations of the stress hormones can cause permanent changes in the cardiovascular system. Numerous research studies linking prolonged anger in particular with CORONARY ARTERY DISEASE (CAD). The suppression of anger can also result in physical manifestations such as chronic HEADACHE, chronic gastrointestinal symptoms such as NAUSEA or DIARRHEA, or clinical DEPRESSION.

The inappropriate expression of anger that involves aggressive or violent words or actions may also risk the well-being of others. Such expressions may include prolonged yelling, throwing things, physically fighting with others, acts of road rage, acts of VIOLENCE, and in other ways lashing out. ALCOHOL abuse and substance abuse often contribute to inappropriate anger or anger expression.

INAPPROPRIATE EXPRESSIONS OF ANGER

getting into fights	hitting
passive–aggressive behavior	persistent yelling or tirades
placing blame	pretending nothing is wrong
reckless or erratic driving	swearing and abusive language
tantrums (at any age)	
throwing or breaking things	

Anger management is the structured effort to express anger in appropriate, constructive ways through learned responses and behaviors. Therapists and psychologists can teach methods to identify circumstances that trigger anger and appropriate ways of expression through approaches that may include

- COGNITIVE THERAPY to change the way a person thinks about anger
- BEHAVIOR MODIFICATION THERAPY to change a person's actions and behaviors
- discussion of underlying worries, fears, and issues that may contribute to feeling angry
- problem-solving and communication skills

People who are unable to control anger and their behavior responses through therapy may have a psychiatric disorder called intermittent explosive disorder, which often improves with selective serotonin reuptake inhibitor (SSRI) medication treatment. The SSRIs are ANTIDEPRESSANT MEDICATIONS that extend the presence of serotonin, a NEUROTRANSMITTER, in the BRAIN. Serotonin is key in the movement of electrical impulses among brain neurons responsible for mood and emotion.

Some people also benefit from alternative and complementary approaches such as HYPNOSIS and BIOFEEDBACK and from relaxation methods including MEDITATION and YOGA. Regular physical exercise reduces stress, provides an outlet for physical tension, and induces the release of endorphins and enkephalins, biochemicals in the brain that cause feelings of pleasure. Health conditions that can cause changes, sometimes sudden, in a person's anger response and anger management ability include serious illness or injury, STROKE, BRAIN TUMOR, degenerative neurologic conditions such as ALZHEIMER'S DISEASE, and TRAUMATIC BRAIN INJURY (TBI).

See also CHILD ABUSE; DOMESTIC VIOLENCE; ELDER ABUSE; EXERCISE AND HEALTH; PROBLEM-SOLVING AND CONFLICT RESOLUTION; STRESS AND STRESS MANAGEMENT.

C

child abuse Actions by parents and other caregivers that endanger a child's physical and emotional well-being. Child abuse affects about 1 million children in the United States each year, 1,200 of whom die as a result of the abuse they experience. In many countries child abuse is both a health concern and a legal matter. In the United States federal law establishes basic legal criteria that define child abuse; each state further describes the actions that meet such criteria and may extend the criteria to include additional circumstances of abuse. There are four basic types of child abuse:

- Neglect occurs when the parent or caregiver fails to provide for the child's basic needs such as appropriate nutrition, clothing, shelter, medical care, and physical and emotional attention. Examples of neglect include grossly unsanitary living conditions, persistently depriving a child of meals, locking a child in a room or out of the house, and leaving a child alone and unattended for extended periods of time.
- Physical abuse occurs when a child receives injuries, regardless of whether the parent or caregiver intended to cause harm. Examples of physical abuse include harsh physical discipline, hitting, shaking, kicking, and choking.
- Sexual abuse occurs when there is inappropriate physical contact of a sexual nature between a parent or caregiver and the child. Examples of child sexual abuse include fondling, indecent exposure, incest, and rape.
- Emotional abuse occurs when the words or actions of the parent or caregiver impair the child's sense of self and value. Examples of emotional abuse include persistent threatening, yelling, criticizing, and ostracizing.

Typically an abused child experiences more than one type of abuse; emotional abuse is nearly always a component of any other type of abuse. Child abuse may also occur when parents or caregivers fail to take action to prevent harm or injury to the child, including intervening to stop the abusive actions of another parent or caregiver.

Signs of Child Abuse

Indications of child abuse may be physical or behavioral. Signs that suggest neglect and child abuse include

- unexplained bruises, BURNS, fractures, or other physical injuries
- weight and size significantly less than appropriate for age
- steals food or has an extremely unhygienic appearance
- flinching, ducking, and other fearful behavior in response to sudden movements from adults
- nightmares and unusual fears
- inappropriate sexual knowledge or behavior
- symptoms of SEXUALLY TRANSMITTED DISEASES (STDS)

A sudden, unexplainable change in a child's behavior is a warning sign that bears investigation because it can indicate any number of serious issues, from abuse to physical illness to ILLICIT DRUG USE. A child often will not acknowledge that a parent or caregiver is abusive. Children depend on their caregivers and may fear retribution from the abuser or may not recognize that the behavior or situation constitutes abuse. As well, secrecy is often a key component of abuse, with the abuser

threatening the child with harm should he or she say anything to others about the abuse.

It is crucial that anyone who suspects a child is being abused, regardless of the person's relationship to the child, notify a health-care provider or other authority. Many communities have anonymous telephone hotlines for reporting suspicions of child abuse.

Detection and Intervention

All communities have child protection agencies and legal mechanisms to safeguard the well-being of children. Most states require health-care providers, educators, and other adults who have frequent interactions with children to report any suspicions or signs of child abuse. Child protection authorities then investigate the situation and may remove, temporarily or permanently, an endangered child from an abusive environment or situation. The longer the child remains in the abusive situation, the more serious and long-lasting the physical and especially emotional consequences.

The safety and health of the child is the priority in circumstances of neglect and abuse. However, because not all neglect and abuse is purposeful, parent education programs that teach PARENTING skills as well as nonabusive methods to manage child discipline and the stress of parenting may help a parent or caregiver change his or her behavior such that it becomes appropriately nurturing and supportive.

See also CULTURAL AND ETHNIC HEALTH-CARE PERSPECTIVES; DOMESTIC VIOLENCE; ELDER ABUSE; FACTITIOUS DISORDERS.

cultural and ethnic health-care perspectives Awareness of, respect for, and accommodation of the traditions, beliefs, and customs of diverse cultures and ethnicities within the conventional practice of medicine. Factors may include language (non-English speaking), immigration status, views about doctors and personal privacy, and the influence of religious or spiritual beliefs as they relate to the reasons for illness and the role of treatment.

The American model of medicine encourages shared participation between health-care providers and patients. This model expects patients to question what they do not understand. People from some cultures may expect the provider will choose the appropriate therapy and are reluctant to ask any questions. In other cultures families make decisions about health care, sometimes without participation from the person who is receiving the care. These factors influence patient compliance—whether the person carries out the treatment the doctor or other health-care provider recommends. The American model of medicine also has a relative openness about personal privacy and the sanctity of the body, facets of health care that are often distressing or offensive to people of other cultures who may refuse diagnostic or therapeutic procedures unless providers are able to accommodate their customs and beliefs.

Cultural competency is now part of education and training for many health-care professionals in the United States, including physicians, physician assistants, nurses, dentists, and allied health staff. Nearly all hospitals have translators available to overcome language barriers. About 18 percent of the population in the United States speaks a primary language other than English, and cultural and ethnic minorities collectively make up about a third of the US population.

See also AYURVEDA; GENERATIONAL HEALTH-CARE PERSPECTIVES; NATIVE AMERICAN HEALING; SPIRITUAL BELIEFS AND HEALTH CARE; TRADITIONAL CHINESE MEDICINE (TCM).

D–E

domestic violence Actions and behaviors that use aggression, threats, and fear to control another person in a household or partner relationship such as a marriage or dating. Domestic VIOLENCE has health as well as legal ramifications. In the United States, state laws define the parameters of behaviors that constitute domestic violence.

The National Domestic Violence Hotline—1-800-799-SAFE (7233)—is available tollfree, 24 hours a day, seven days a week, from anywhere in the United States.

Each year more than four million American women seek medical care for injuries resulting from domestic violence. However, either partner may be the abuser. Domestic violence can exist in any domestic partnership, including marriage, nonmarried partners, same-sex partners, and dating. Surveys among American high school and college students suggest violence among dating couples, such as hitting and forced sex, is a serious issue.

Signs and indications of domestic violence in a partnership may be emotional, psychologic, physical, or a combination. Such signs may include

- behaves in a jealous and possessive manner
- attempts to isolate partner from family and friends or monitor visits and activities
- controls finances and other resources such as car keys
- constantly criticizes, uses name calling, and humiliates
- threatens or carries out physical harm to partner, children, friends, or pets
- acts abusively or forcefully in sexual situations; demeans partner
- persistently yells or argues; breaks items in the house

The priority in domestic violence is for the abused person to get away from the situation, which is often difficult. There are the emotional ties of the relationship, however dysfunctional, as well as the practical matters of resources and where to go. Some people are able to go temporarily to the homes of other family members or friends, though sometimes others who know of the violence are reluctant to become involved. More often the circumstance is that the abused person has told no one of the situation and is not willing to do so until a crisis precipitates action. Most communities have public and private agencies and services to support people who are leaving circumstances of domestic violence. Permanent solutions in circumstances of persistent or severe domestic violence are difficult and often require filing appropriate criminal charges against the abuser as well as relocating and re-establishing work and life.

See also ANGER AND ANGER MANAGEMENT; CHILD ABUSE; ELDER ABUSE.

elder abuse Actions by caregivers and family members that endanger the health, well-being, and life of an older person. Many though not all older people who are in situations of abuse are weak or debilitated and depend on those who abuse them, making escape from the abuse difficult or impossible. Elder abuse affects more than two million older adults in the United States each year. There are four basic types of elder abuse:

- Neglect occurs when family members or caregivers fail to provide for the elder's daily needs such as meals, appropriate clothing, assistance with bathing and toileting, administration of medications, and receiving medical care.
- Physical abuse occurs when the elder receives injuries or is in physical peril as a result of the actions of family members or caregivers. Examples of physical abuse include hitting, pushing, exposure to water that is too hot or too cold, physical restraints, and overmedication or undermedication.
- Sexual abuse occurs when there is inappropriate physical contact of a sexual nature between a family member or caregiver and the elder. Examples of elder sexual abuse include indecent exposure, touching of the genitals or forcing the elder to touch the caregiver's genitals, rape, and sodomy.
- Emotional and psychologic abuse occurs when family members or caregivers intimidate, threaten, belittle, or ignore the elder. Stealing from the elder, mismanaging finances, and taking over control of possessions such as a home or car are also forms of emotional and psychologic abuse.

Often the elder experiences more than one type of abuse; emotional and psychologic abuse are almost always present with any other type of abuse. Elder abuse may also result from the failure of family members or caregivers to take actions to prevent harm or injury. Though the dynamic of elder abuse is complex, it is nearly always intentional.

Signs of Elder Abuse

Indications of elder abuse may be obvious or discreet and may be physical or manifest as emotional or psychologic symptoms. Signs of elder abuse may be difficult to distinguish from the symptoms and consequences of health conditions such as STROKE or ALZHEIMER'S DISEASE. Signs that may suggest elder abuse include

- unexplained bruises (especially on the wrists, lower arms, and lower legs), BURNS, scalds, fractures, or other physical injuries
- progressive weight loss
- sunken eyes and dry, loose SKIN
- DECUBITUS ULCER (bed sore)
- health conditions that do not respond as expected with the medications prescribed
- vaginal or anal discharge or bleeding
- SYMPTOMS OF SEXUALLY TRANSMITTED DISEASES (STDS)
- evasiveness or reluctance to participate in social activities
- fearfulness or suspicion

Some conditions of old age, such as Alzheimer's disease, ORGANIC BRAIN SYNDROME, and stroke, may result in aggressive, combative, or otherwise challenging behavior in the older person. Such a circumstance complicates the picture by making it difficult to determine who is the abused and who is the abuser. Patterns of abuse present earlier in life, such as DOMESTIC VIOLENCE between spouses or CHILD ABUSE the elder inflicted on a now-adult child, often continue or may reverse when the person becomes older and unable to live independently. The once-abused child may turn against the now-dependent parent, for example.

It is crucial that anyone who suspects elder abuse report it to health-care or law enforcement authorities for investigation. Many communities have anonymous telephone hotlines for reporting suspicions of elder abuse.

Detection and Intervention

Elder abuse is difficult to detect because it is possible for the elder to remain relatively secluded without raising much suspicion. Older people may be reluctant to report abuse for fear of retribution from the abusive family member or caregiver. Elderly people commonly fear any change that might require a move to a residential care center. As well, many older people have well-established beliefs that what happens in the family stays in the family; there would be irrecoverable loss of pride in revealing abuse at the hands of family members. There are relatively few mechanisms in American culture to safeguard the health and

well-being of the elderly, though most states have mandatory reporting requirements for health-care providers and others involved in caring for the elderly when they suspect abuse. When doctors or authorities do detect elder abuse, they often have little choice but to remove the elder from the situation—which is often what the elder fears most. One of the most effective deterrents of elder abuse is social participation—having people visit the older person and getting the older person out to participate in social activities. This approach also provides a break for family members and caregivers, relieving some of the stress that is inherent in providing care for an elder.

See also GENERATIONAL HEALTH-CARE PERSPECTIVES.

end of life concerns The fears and worries that may arise when a person faces the prospect of dying. End of life concerns in regard to health and health care may relate to physical symptoms such as PAIN and loss of function, health-care issues such as feeding tubes and mechanical life support, emotional concerns such as fear of the unknown and leaving loved ones, and legal matters such as medical power of attorney and other advance directives. Cultural and generational factors greatly influence end of life desires and practices, though each person's needs are unique.

The focus of end of life concerns sharpens when a person approaches the end stages of terminal illness. Open communication with health-care providers, family members, and other caregivers establishes clear expectations and intentions around supportive care and medical interventions including pain relief and resuscitative efforts. It also allows a person to make choices and decisions about hospice and other supportive care and to reach closure with loved ones. Sometimes family members have different ideas about what care a loved one might want at the end of life; it is often helpful as well as prudent to put one's wishes in writing.

See also CULTURAL AND ETHIC HEALTH-CARE PERSPECTIVES; GENERATIONAL HEALTH-CARE PERSPECTIVES; GRIEF; QUALITY OF LIFE; SPIRITUAL BELIEFS AND HEALTH CARE.

G–I

generational health-care perspectives Awareness of, respect for, and accommodation of the different viewpoints toward health care across generations. Each generation has inherently different expectations around what medical care can accomplish as well as how doctors and hospitals should provide such care. These differences in expectations shape the nature and outcome of many medical interventions, from preventive to therapeutic efforts. Health-care providers must consider these differences when evaluating treatment options and approaches.

People who are today in their 80s lived much of their lives in a time when medical care was limited and doctors came to them to provide care. Most of the drugs, surgical operations, and technologies that are the mainstay of medical treatment today were developed after 1950 and many only since the 1980s. The elderly may view illness as inevitable to certain degree, expect the doctor to take a leadership role in health care, and be unknowledgeable about the ways in which lifestyle influences health and illness.

By contrast, people who are today in their 30s have lived all of their lives in a time in which medicine prevents many of the illnesses that were common causes of death in earlier generations and treats or cures nearly every sort of illness and injury. They have grown up knowing of the health significance of lifestyle factors such as diet, exercise, and cigarette smoking. They may view illness as either avoidable or curable and expect to participate in considering options and making decisions about their health care.

The structure of the practice of medicine to some extent supports generational separations through its model of specialization. The very young—the newest generation—see health-care providers who specialize in meeting the unique needs of infants and children (pediatricians). These doctors and other health-care providers are often around the same age as the parents—the middle generations—and can personally identify with some of the life circumstances and issues they face. The very old—the oldest see health-care providers who similarly specialize in treating health conditions common in or unique to aging (geriatricians). These health-care providers are often significantly younger than the patients they treat and have little personal identification with their perspectives and life circumstances.

Generational perspectives and perceptions influence the point at which an individual will seek medical care for a health concern, which may have significant effect on the outcome of treatment. Many health conditions, from DIABETES to CARDIOVASCULAR DISEASE (CVD) to cancer, are treatable or curable with early diagnosis and treatment. Generational views on what information is private and personal also affect health outcomes.

See also ANTIBIOTIC MEDICATIONS; CULTURAL AND ETHNIC HEALTH-CARE PERSPECTIVES; SPIRITUAL BELIEFS AND HEALTH CARE; VACCINE.

grief Emotions and feelings, often intense, of irretrievable loss. Grief may be a response to the loss of a loved one through death or the end of a relationship or to the diagnosis of a health condition that signifies the end of a certain way of living. It is natural and normal for people to mourn losses of function, potential, and other aspects of their own health as well as to grieve the prospect of their own impending deaths. Some people also experience grief during significant life transitions, such as when a child leaves home.

Though the grieving process, also called bereavement, consists of predictable kinds of responses and feelings, each person handles grief uniquely. The range of emotions associated with grief includes sadness, anger, disbelief, denial, despair, numbness, and guilt. A person may experience some or all of these emotions at varying intensities and periods of time. Grief can be overwhelming and incapacitating, particularly at its onset and in circumstances of unexpected loss. Grief is also important for HEALING from the sense of loss.

A person who is grieving may appreciate support and comfort from others or may prefer to grieve in private. It is important for the grieving person to know others are there, however. Rituals such as funeral ceremonies are among the ways societies deal with grieving in communal ways. Age, culture, and spiritual beliefs are among the many factors that influence the expression and process of grieving.

See also DEPRESSION; END OF LIFE CONCERNS; INTERPERSONAL RELATIONSHIPS; SPIRITUAL BELIEFS AND HEALTH CARE.

interpersonal relationships The partnerships and associations people form with other people. These may include family, friendship, intimate, sexual, workplace, and social relationships. Though the need to socialize is universal, individuals and cultures approach social bonds in different ways. Some people prefer a few close individual partnerships that have a fairly substantial degree of intimacy. Other people prefer to socialize with groups in which there is no distinct pairing or partnering. Such group relationships often form around common interests, ranging from sports and recreational activities to religious beliefs and intellectual or educational pursuits. Gender and generation also influence the ways of socialization and the nature of relationships.

Whatever their configuration, interpersonal relationships are essential for emotional and psychologic health and often also for physical well-being. Numerous studies show that people who live in isolation are more likely to develop psychologic conditions such as depression as well as physical health problems. The romanticized notion that one could die of a broken HEART becomes substantiated in reality in situations when people lose their longtime partners, particularly men whose wives die before them. Studies show that even interaction with pets improves emotional stability and satisfaction with life.

Intentional deprivation of interpersonal relationships, such as may occur with CHILD ABUSE, can cause lifelong and sometimes irreparable psychologic damage that inhibits the ability to form friendships and intimate partnerships. Relationships with parents and siblings are the first to form. Family life provides early guidance and teaches the skills a person needs to develop relationships outside the circle of family.

See also AUTISM; DOMESTIC VIOLENCE; ELDER ABUSE; PEER PRESSURE; PROBLEM SOLVING AND CONFLICT RESOLUTION; QUALITY OF LIFE.

P

parenting The functions and processes of raising a child. Most people grow and change in their roles as parents as their children also grow and change. Parents learn from their experiences and their mistakes. Though one's own parents are often the most dominant role models for parenting, new understandings about childhood development may emphasize a different approach or set of skills for parenting today.

Numerous classes and programs are available—many of which community agencies offer at little cost or no cost—that teach effective parenting skills, appropriate discipline methods, and ways for coping with the unique stresses of each developmental stage from infancy through ADOLESCENCE. Friends and peers who are also raising children often provide alternative ways of looking at and handling specific though universal situations such as tantrums, defiant behavior, dating, and driving.

KEY PARENTING RESPONSIBILITIES

- provide a loving, nurturing, safe environment
- provide adequate nutrition and physical activity
- provide appropriate medical care and dental care
- establish expectations and enforce limits
- listen and respond to the perspectives and concerns the child expresses
- seek help when things get out of hand
- encourage appropriate achievement and express pride in accomplishments

Just as there are stages of development for children, there are periods of learning and changing for parents. The needs of children shift as they grow and mature, and it is important for parents to adapt to support and accommodate those shifts and the child's increasing independence. Parents need to relearn supervision and discipline approaches to provide appropriate guidelines with each developmental shift. It is important for parents to be aware of activities in which children may engage that put them at risk. The increasing mobility and technology of the current culture, coupled with the reality that more children than not today grow up in what earlier generations would have perceived as nontraditional households, allows greater independence and access at an earlier age.

Parents also need to balance their careers and social interests with the demands of parenting. It is important for parents to maintain time for their partners and friends, though this is often a challenging and sometimes daunting goal, because it helps them maintain balance overall. It is also important for parents to be able to have time away from their children. As well, staying with other adults helps children develop comfort in knowing their parents can leave and will return.

Many parents worry that they do not give enough of themselves to the functions of parenting, particularly when behavior problems arise. However, behavior is fluid and dynamic and nearly all children engage in some behaviors that distress their parents, teachers, and sometimes even their own friends and peers. Most child development experts agree that whatever the parenting style, flexibility and the ability to "go with the flow" for at least a short time are approaches that help children to find their bearings and move on to more appropriate behaviors. Exceptions, of course, are behaviors that threaten the safety and well-being of the child or others, circumstances that require immediate and appropriate intervention.

See also CHILD ABUSE; INTERPERSONAL RELATIONSHIPS; STRESS AND STRESS MANAGEMENT; WORKPLACE STRESS.

peer pressure The influences of friends, acquaintances, colleagues, and co-workers. Peer pressure may be positive or negative. Though the common perception of peer pressure is of a childhood and ADOLESCENCE phenomenon, the attitudes and actions of others remain influential to varying degree throughout life. One's peers—those with whom a person feels relatively equal—are instrumental in shaping compliance with societal norms and behavioral standards. In the workplace peer pressure becomes the corporate culture, for example. Peer pressure is also a pivotal component of the "one for all" dynamic of military training and performance.

Even in adolescence, a time when individuals are particularly concerned about fitting in and behaving the same as everyone else, peer pressure is more often positive than negative. Friendships, because they develop from shared interests, often reinforce values and behaviors that are desirable within the context of community or family ideals and expectations.

Peer pressure becomes problematic when it induces individuals to think and behave in ways that have negative or adverse consequences. Negative peer pressure may manifest as experimentation with ALCOHOL or ILLICIT DRUG USE, criminal activity, or socially unacceptable attire and appearance. Such manifestations are most common in adolescence because it is a time of vulnerability and searching for self-identity, but it may occur at any point in life. Corrupt and illegal actions within corporations, which periodically become prominent, represent negative peer pressure as well.

Peer pressure is unavoidable. It is a dynamic that shapes conformity with group, societal, and cultural expectations. The key is for individuals to have a strong enough internal framework of integrity to know when those expectations are inappropriate and to be able to stand apart from them when they are.

See also PROBLEM SOLVING AND CONFLICT RESOLUTION; YOUTH HIGH-RISK BEHAVIOR.

problem solving and conflict resolution Skills and methods to resolve differences between individuals and among groups. The essence of problem solving and conflict resolution is to find common ground—shared values, beliefs, goals, intentions, and expectations. From such a platform it is often possible to resolve differences.

There are numerous methodologies for problem solving and conflict resolution, the appropriateness of which depends on the setting and circumstances. Conflicts in the workplace require a different focus from problems in the classroom or challenges in the family, even though the underlying challenges are similar. Regardless of methodology, there are some basic steps common to nearly all settings:

- Isolate the problem: What—not who—accounts for the differences that are creating disagreement and conflict?
- Establish a common base of expectation for resolution: What will improve the situation?
- Agree on steps that will move all parties toward resolution: How will the situation improve?
- Implement the steps, along with a process for assessing the success of each step.
- Reevaluate: Does the solution solve the problem or resolve the conflict?

Personalities and personal agendas often get in the way of objective conflict resolution. It is important to recognize, however, that it is attitudes, behaviors, and actions that are responsible for conflict. These factors are within the ability of an individual to change. People are more willing to make changes when they are able to see the outcome as gaining rather than giving up.

See also ANGER AND ANGER MANAGEMENT; STRESS AND STRESS MANAGEMENT; WORKPLACE STRESS.

S

sexual assault Unwilling, unconsenting, or forced sexual interaction. Sexual assault involves implied or actual use of VIOLENCE to force compliance and is an act of violence, not an act of sexual gratification. Sexual assault is also criminal act and has potentially serious health consequences. Rape is sexual assault in which there is attempted or completed penetration of the VAGINA, ANUS, or MOUTH by the PENIS, finger, or an object. In some states the legal term for penetration other than vaginal is *sodomy.* Incest is sexual assault in which the perpetrator is a family member and may occur as a form of CHILD ABUSE.

Women, men, and children may be the victims of sexual assault. Those at highest risk are women between the ages of 16 and 20. About 100,000 sexual assaults are reported to police in the United States each year, which health experts believe represents perhaps only 1 in 4 of sexual assaults that actually occur. Sexual assault in which the victim is male is even less frequently reported.

Legal Issues of Sexual Assault

Though it is a natural desire to immediately bathe or shower after a sexual assault, it is crucial to first seek medical attention. SEMEN and other bodily fluid samples are essential for identifying the perpetrator of the assault, even when the victim knows the assailant. Hospital emergency departments often have staff (sexual assault nurse examiners) who have special training in obtaining such samples and conducting sexual assault examinations that are in compliance with the standards of legal evidence. Most hospitals have sexual assault advocates and support services they contact who can provide assistance for the victims of sexual assault.

Health Issues of Sexual Assault

Traumatic injury resulting from forceful penetration, SEXUALLY TRANSMITTED DISEASES (STDS), unwanted PREGNANCY, and emotional trauma are the key health issues of sexual assault. Doctors may recommend or administer (with consent) emergency CONTRACEPTION when pregnancy is a possibility. Doctors also typically offer ANTIBIOTIC PROPHYLAXIS as a defense against STDs, with recommended follow-up testing for STDs that have longer incubation periods or are viral, such as HEPATITIS, HIV/AIDS, SYPHILIS, and GONORRHEA.

The emotional consequences of sexual assault can be long lasting and significant. Doctors recommend counseling even when the person does not feel it is necessary. ACUTE STRESS DISORDER and POSTTRAUMATIC STRESS DISORDER (PTSD) are common. Sexual assault may result in prolonged inability to form intimate relationships or enjoy sexual partnerships, either in existing circumstances such as marriage or in subsequent circumstances.

Risk Reduction Measures

Because sexual assault is a criminal act of violence that is often random, it is not possible to completely prevent attack. However, law enforcement officials recommend these measures to reduce the risk for sexual assault

- maintain high awareness of one's surroundings, particularly during times of darkness (including early morning hours especially in the winter)
- when walking alone, walk at a purposeful stride and in the center or closer to the curb side of sidewalks
- do not enter a car, home, or other setting if anything about it seems suspicious

- do not consume so much ALCOHOL when out with a group or on a date that it impairs one's ability to take action to stop unwanted sexual advances
- do not accept or consume "party drugs"

See also DOMESTIC VIOLENCE; ELDER ABUSE; GAMMA HYDROXYBUTYRATE (GHB).

sexual orientation A continuing or enduring physical and emotional attraction and sexual interest in another person. Most health experts view sexual orientation as a continuum with exclusive heterosexuality (attraction only to people of the opposite sex) at one end and exclusive homosexuality at the other end (attraction only to people of the same sex). Along the continuum are varying degrees of mixed attraction (heterosexual and homosexual), often called bisexuality. Sexual orientation is distinct from an individual's sexual identity and perceptions of SEXUALITY.

Most researchers believe sexual orientation develops in early childhood as a complex interaction of numerous psychologic, biologic, and behavioral factors. However, some researchers believe sexual orientation is purely biologic or genetic, and others maintain that it is purely behavioral. Within these attempts to understand and explain sexual orientation, nearly all researchers agree that whatever its origins, sexual orientation is not a matter of choice. The basis for this agreement is the recognition that sexual orientation emerges before sexual exploration.

The American Psychological Association, American Psychiatric Association, American Counseling Association, and other organizations of health-care professionals affirm that sexual orientation, no matter where it is along the continuum of possible expressions, is simply a dimension of individual experience and definition and adamantly oppose efforts to change sexual orientation (notably homosexuality) through therapy and refute claims that therapy can accomplish such an objective. Rather, mental health professionals hold that the purpose of therapy related to sexual orientation is to help an individual who is uncomfortable with his or her sexual orientation reach a level of understanding and acceptance about it, which may include choices around how to accommodate sexual orientation issues and whether to engage in intimate relationships.

See also INTERPERSONAL RELATIONSHIPS; SEXUAL HEALTH.

sexuality A person's overall attitudes, perceptions, and expressions of sexual identity, SEXUAL ORIENTATION, and sexual behavior, intimate relationships (whether or not those relationships include sexual activity). The organs of reproduction provide the physical basis for gender and sexuality. Other factors, from genetics to biochemistry, add further layers of complexity so that sexuality becomes a fundamental element of human existence along the entire continuum of life. Sexuality plays a significant role in self-esteem and self-confidence, shaping how people perceive themselves, and how they present themselves to others.

Numerous health circumstances affect sexuality, from physical development and aging to injury and illness. Changes in the body's physical appearance shift awareness of sexuality at key life passages such as PUBERTY, PREGNANCY, and MENOPAUSE. Health conditions that affect physical function may affect an individual's interest in or ability to participate in SEXUAL INTERCOURSE and other sexual activity. Among such health conditions are OBESITY, DIABETES, CARDIOVASCULAR DISEASE (CVD), neurologic disorders, STROKE, HEART ATTACK, and CHROMOSOMAL DISORDERS such as TURNER SYNDROME and KLINEFELTER SYNDROME. Because the base of sexuality is inherently linked to the organs of reproduction, conditions (and their treatments) that affect those organs are often especially challenging to sexuality. Treatments that result in physical alterations of the body, such as AMPUTATION and MASTECTOMY, often affect the person's perceptions about his or her physical attractiveness and sexual desire.

See also AGING, REPRODUCTIVE AND SEXUAL CHANGES THAT OCCUR WITH; ERECTILE DYSFUNCTION; INTERPERSONAL RELATIONSHIPS; LIBIDO; SEXUAL DYSFUNCTION; SEXUAL HEALTH.

spiritual beliefs and health care The influences of an individual's faith on health-care decisions and outcomes. Spirituality is the sense of how one fits within and relates to the scheme of existence,

helping define such concepts as the purpose of life. Interactions between the sense of spirit, the mind, and the body provide powerful connections that shape the experiences and expressions of health and well-being as well as of illness and injury.

Faith is often the factor that provides comfort during health crises and confidence that treatment will succeed. Numerous studies show correlations between positive outcomes in serious illness or injury and directed manifestations of belief such as prayer circles, HEALING ceremonies, and spiritual rituals. In some cultures spiritual practices are inseparable from healing. A person's faith or religion (a particular belief structure) may also be the source of acceptance in chronic or terminal health conditions.

As well, religious or spiritual beliefs may guide the kinds of health-care decisions, including diagnostic procedures and treatments, individuals make. For example, a religion's doctrines may proscribe FERTILITY testing, CONTRACEPTION, or the receipt of donor BLOOD (BLOOD TRANSFUSION) or organs.

See also AYURVEDA; CULTURAL AND ETHIC HEALTH CARE PERSPECTIVES; MEDITATION; MIND–BODY CONNECTION; NATIVE AMERICAN HEALING; PRAYER AND SPIRITUALITY; TRADITIONAL CHINESE MEDICINE (TCM).

stress and stress management Stress is any factor that alters equilibrium. Stress management is the effort to manage stress to maintain equilibrium. Stress is a constant and necessary dimension of life. Stress can be physiologic, psychologic, or emotional and often exists in combination.

Physiologic stress maintains vital bodily functions such as BREATHING, HEART RATE, and BLOOD PRESSURE. The STRESS RESPONSE HORMONAL CASCADE instigates the "fight or flight" response that mobilizes the body's resources. The key HORMONE of this cascade is CORTISOL, which the ADRENAL GLANDS secrete. Cortisol influences or regulates numerous physiologic functions, either directly or through the release or suppression of other hormones such as EPINEPHRINE and NOREPINEPHRINE. It also initiates HEALING, stimulating the IMMUNE RESPONSE, and focuses NEUROTRANSMITTER release and NEURON communication in the BRAIN to intensify cognitive function.

The Health Consequences of Excessive Stress

Stress becomes problematic for health when it exists in excess for an extended time. Sustained elevation of the stress hormones damages cells, tissues, and organs throughout the body, most notably those of the cardiovascular system. Indications of prolonged, excessive stress may include

- irritability, moodiness, or outbursts of anger
- worry, crying, or panic attacks
- difficulty sleeping, sleeping too much, or feeling that sleep is not restful
- PALPITATIONS
- frequent HEADACHES
- gastrointestinal distress such as NAUSEA, VOMITING, or DIARRHEA
- increased APPETITE or loss of interest in eating

Elevated cortisol alters the body's ability to produce and use INSULIN, which affects METABOLISM of lipids. Researchers believe this contributes to HYPERLIPIDEMIA and resulting ATHEROSCLEROSIS and may play a role in the development of type 2 DIABETES. Excessive stress may also exacerbate chronic health conditions such as HYPERTENSION (high blood pressure), INFLAMMATORY BOWEL DISEASE (IBS), MULTIPLE SCLEROSIS, PARKINSON'S DISEASE, and DIVERTICULAR DISEASE.

Inappropriate Stress Relief Efforts

People sometimes turn to ALCOHOL, cigarette smoking, and drugs (legal as well as illicit) to relieve stress. Though these approaches may provide relief in the short term, they can have numerous adverse effects on health over the long term. Alcohol is a mild depressant, acting to slow NERVE impulses and neuron function in the brain. Though occasional and moderate alcohol consumption does not present health issues for most people, long-term use of alcohol for stress reduction is both counterproductive and damaging to health. Chronic alcohol consumption has numerous deleterious effects on the body, from LIVER and nerve damage to increased risk for STOMACH CANCER, LIVER CANCER, cognitive dysfunction, memory impairment, and impaired healing. Tobacco, though regular smokers feel it calms them, contains NICOTINE, a powerful and addictive stimulant.

The calming effect of smoking a cigarette is more that of quieting the addictive need than genuine relaxation.

Methods to Manage Stress

The most effective means of managing excessive stress is to reduce its sources to the extent possible. This may require evaluation of the demands of work, family, and other commitments to prioritize them. Much excessive stress results not so much from an individual source but from the cumulative effects of multiple demands. Sometimes simply the process of evaluation reveals potential for change. Though it may not be possible to eliminate the source of the stress, it often is possible to mediate, through various techniques, its ability to cause stress. A key dimension of stress management is the ability to gain control over the circumstances of stress, including personal responses to it.

EFFECTIVE METHODS FOR STRESS RELIEF

ACUPUNCTURE	AROMATHERAPY
BIOFEEDBACK	BREATHING EXERCISES
COGNITIVE THERAPY	LABYRINTH
MEDITATION	physical exercise
prayer	TAI CHI
VISUALIZATION	YOGA

See also ACUTE STRESS DISORDER; ALCOHOLISM; COGNITIVE FUNCTION AND DYSFUNCTION; GENERALIZED ANXIETY DISORDER (GAD); MEMORY AND MEMORY IMPAIRMENT; POST-TRAUMATIC STRESS DISORDER (PTSD); WORKPLACE STRESS.

support groups People who have in common specific health-care conditions, either as patients or family members and caregivers, who meet to provide information and a safe environment for dialogue about fears, worries, expectations, and other concerns. Hospitals and health organizations often maintain support groups, providing meeting space, structured meeting times, and sometimes a doctor, nurse, therapist, or other health-care provider to serve as moderator or host when the group meets. Other support groups are casual and may meet in a member's home or social setting on either a regular or an ad hoc (as-needed or spontaneous) basis.

A less traditional though sometimes more accessible type of support group is one that communicates through Internet forums and message boards. Such online venues allow people to share their comments and questions any time. Some also feature scheduled presentations from specialists who provide information and answer questions.

See also PSYCHOTHERAPY; STRESS AND STRESS MANAGEMENT.

V–W

violence Actions of aggression that cause intentional harm to others. Violence may be targeted or random and may occur in the workplace, at school, or in the home (DOMESTIC VIOLENCE). Violence is a leading cause of injury and death in the United States, accounting for nearly two million hospital emergency visits and 20,000 deaths a year. Homicide is also the leading cause of death among pregnant women, claiming about 2,000 lives each year.

Those most vulnerable to injury and death due to violence are young people, primarily men, between the ages of 15 and 24, for whom homicide is the second leading cause of death (and leading cause of death among African Americans). Firearms (mostly handguns) account for nearly two thirds of all homicides in the United States. The most common form of violence against young people is date violence—actions such as hitting, choking, and forced sex. Youth gangs are also often violence oriented.

The long-term consequences of violence include physically disabling health conditions such as TRAUMATIC BRAIN INJURY (TBI) and SPINAL CORD INJURY, which often result in permanent BRAIN damage or PARALYSIS. Psychologic conditions such as ACUTE STRESS DISORDER, DEPRESSION, GENERALIZED ANXIETY DISORDER (GAD), PHOBIA, and POST-TRAUMATIC STRESS DISORDER (PTSD) are also common among people who have experienced violence.

Efforts to reduce violence include recognition of warning signs that a person may be inclined toward violence or is planning an act of violence. Such signs may include

- outbursts of extreme anger or rage
- talk of committing acts of violence
- possession of weapons or destructive devices
- punching, hitting, or choking others in "fun"
- disparaging attitudes and comments toward individuals, ethic groups, or organizations (such as schools, employers, or the government)

Depending on the person's behavior, age, and other circumstances, the appropriate authorities may be able to intervene to thwart potential acts of violence. PSYCHOTHERAPY and BEHAVIORAL MODIFICATION THERAPY may help individuals replace violent reactions and behaviors with behaviors that are more appropriate; therapy can help individuals understand what causes the feelings of frustration or anger that are often behind their violent actions. Psychotherapy and COGNITIVE THERAPY may help people who have experienced violence to develop constructive COPING MECHANISMS.

See also ACCIDENTAL INJURIES; ANGER AND ANGER MANAGEMENT; CHILD ABUSE; ELDER ABUSE; SEXUAL ASSAULT; STRESS AND STRESS MANAGEMENT; SUICIDE IDEATION AND SUICIDE.

workplace stress Tension and pressure among co-workers in the work environment or within individuals as a consequence of work demands. In the work environment people must work together, often in collaborative ways, with people they might otherwise not associate. Though many employers attempt to foster good relationships among employees, co-workers may have little in common beyond specific work qualifications and job skills. More than 25 percent of workers in the United States consider work the most significant source of stress in their lives. About 60 percent of work absenteeism is directly attributable to stress.

Issues in the workplace may include co-workers who do not get along with one another, people who do not pull their share of the workload,

heavy workloads, tedious or repetitious work, demanding customers, and short staffing. As well, people may work in jobs that are not a good match for their needs and interests—because such a job may pay more than a better-suited job, offer more lenient time away to deal with children, have health insurance benefits the person or family needs, or be the only work available in a particular location. Physical danger inherent in certain jobs also establishes a high level of emotional stress.

FACTORS THAT CONTRIBUTE TO WORKPLACE STRESS

automation
child care issues
complex, time-sensitive work tasks
co-worker conflict
downsizing and corporate restructuring
family demands
heavy workload
inability to make decisions about work tasks
lack of privacy
noisy work environment
repetitious or tedious work
work unsuited to interests

Work responsibilities are often in direct competition with family responsibilities for a person's time and interest. About 40 percent of American families have only a single parent, resulting in significant stress around child care arrangements and expenses. Even among families in which both parents work, parents find it necessary to juggle work responsibilities and child needs such as illness, health-care appointments, and school activities.

Unmitigated work stress has numerous consequences for both physical and psychologic stress. Stress-related physical conditions may include frequent headaches, IRRITABLE BOWEL SYNDROME (IBS), and ACCIDENTAL INJURIES. Work stress may also contribute to various psychologic conditions in which stress is a significant factor. An extreme of work stress is burnout, in which a person may experience symptoms such as PALPITATIONS, trembling, sleep disturbances, and unprovoked outbursts of anger.

The most effective solutions for work stress combine changes in the work setting with stress management methods. Many people may benefit from career counseling to help them determine what kinds of work or jobs might be more appropriate for their interests and abilities. Sometimes it is necessary to change jobs to relieve work stress. Other approaches may include identifying one specific problem at work that causes stress and coming up with possible solutions.

See also ANGER AND ANGER MANAGEMENT; OCCUPATIONAL HEALTH AND SAFETY; SOMATIZATION DISORDER; STRESS AND STRESS MANAGEMENT; VIOLENCE.

SURGERY

Surgery is the specialty within the practice of medicine in which its practitioners use instruments, devices, and techniques to repair or remove organs and structures affected by congenital defect, injury, or disease processes. Surgical operations are invasive—that is, they enter or open the body in some way.

Two health-care disciplines merge within the arena of surgical operations: ANESTHESIA and surgery. Physicians who administer anesthesia are anesthesiologists (MDs or DOs). Registered nurses who have advanced practice education and certification in anesthesiology are certified registered nurse anesthetists (CRNAs). Anesthesiologists may also choose to further specialize in PAIN management care.

Physicians who perform surgical operations are surgeons, with further designation according to the surgeon's subspecialization. For example, a surgeon who operates exclusively on structures of the chest except the HEART is a thoracic surgeon; a surgeon who operates exclusively on the heart is a cardiac surgeon. A surgeon who operates exclusively on bones and joints is an orthopedic surgeon.

This section, "Surgery," presents an overview discussion of the concepts and practices of surgery and general entries about surgical operations and their role in diagnosis and treatment of diseases, congenital anomalies, and injuries. Entries about specific operations are in the sections that discuss the relevant body system—for example, the entry for HYSTERECTOMY (an OPERATION to remove the UTERUS) is in the section "The Reproductive System" and the entry for CHOLECYSTECTOMY (an operation to remove the GALLBLADDER) is in the section "The Gastrointestinal System."

Surgery Comes of Age

Early documents from diverse cultures provide evidence that surgery—entering the body for therapeutic purposes—has long been among the treatment options of physicians. Ancient Ayurvedic physicians extracted cataracts, amputated limbs, delivered babies by CESAREAN SECTION, drained pus from infected wounds, removed bladder stones, and even performed what plastic surgeons today call pedicle flap tissue grafts to repair damaged noses. Greek physicians operated on soldiers to repair battle wounds. In Babylonia and Egypt surgeons were distinct from physicians, with clearly defined duties and responsibilities.

Toward the end of the 19th century vastly improved understanding of anatomy (the body's structure) and physiology (the body's functions) encouraged physicians to explore the intentional opening of the body to remove tumors and repair damage such as from injury or disease. Nearly all of the misconceptions perpetuated through centuries evaporated in the evidence researchers acquired through scientific study and dissection of human cadavers. Surgeons boldly ventured into new territory: the inner body. Unfortunately, though surgeons had the knowledge their patients were less than eager to allow its display. Few willingly submitted to the scalpel when the only escape from pain was a fortuitously well-placed upper right to the jaw that delivered UNCONSCIOUSNESS. As well, more people died of INFECTION after surgery than recovered from the operation.

But in the 20th century two advances in medicine converged to make surgery feasible: antisepsis and anesthesia. As a result of these two crucial developments, today surgery is the treatment of

first choice for numerous health circumstances. Surgical operations can restore and improve function, improve appearance, repair the damage of traumatic injury, replace dysfunctional organs and structures, remove tumors and infected tissue, and correct potentially life-threatening congenital anomalies. Surgeons in the United States perform more than 25 million operations a year.

SURGERY NOMENCLATURE: TYPES OF OPERATIONS

Term Ends In	Operation Is to
-ectomy	remove a body part or segment of tissue
-ostomy	establish a passage between two structures
-otomy	open an area of the body
-plasty	repair or reconstruct a body part

Anesthesia: Making Surgery Painless

Until the middle of the 19th century surgery was a treatment of last resort, chosen only when the only alternative was certain death. The most effective, albeit unpredictable, anesthesia was a surprise uppercut punch to the jaw that could render a person unconscious long enough for a fast surgeon to complete an operation such as extraction of a bullet or AMPUTATION of a limb. ALCOHOL and opium were the drugs of choice for postoperative pain relief.

The first effective anesthetic agent was ether, administered by having the person breathe fumes as they evaporated from a saturated cloth. Though chemists had compounded ether (sulfuric acid distilled in alcohol) since the 13th century and explored it as a solvent and a sedative for centuries, its properties as an anesthetic did not become known until chemistry students in the early 1800s began using it for entertainment at parties. Their instructors observed that the more ether a person inhaled, the more impervious he or she was to pain. But not until the middle of the century did surgeons begin to explore using ether to intentionally intoxicate an individual to create a state of unconsciousness. In 1842 American physician Crawford Long (1815–1878) used ether to anesthetize a friend, then surgically removed several cysts from the friend's neck. The friend felt no pain and had no memory of the surgery.

Discoveries of similar properties for chloroform and nitrous oxide rapidly expanded anesthesia options. These substances were more effective and less noxious than ether and soon displaced it for operations and dental procedures. Over the latter decades of the 19th century surgeons refined the mechanisms for delivery of anesthetic agents to provide relatively predictable and safe anesthesia during surgery. In the 1880s surgeons experimenting with controlled delivery of anesthetic agents had developed valve-controlled inhalers and the precursor of the endotracheal tube, a tube inserted into the trachea with an air-filled cuff on the end to hold it in place and seal the trachea. By 1930 endotracheal intubation had become the standard method for administering inhalation anesthesia, as it remains today.

Modern anesthetic agents are faster acting, more specific in the effects they achieve, and much safer than their predecessors. Though unpleasant side effects remain possible, anesthesia for most people accomplishes precisely and only the intended purpose. Anesthesiologists and certified nurse anesthetists (physicians and registered nurses, respectively) who specialize in the delivery of anesthesia, carefully administer anesthesia tailored to each individual patient's needs and health circumstances.

Antisepsis: Making Surgery Safe

Though surgeons knew all too well the high rate of death after surgery, it was an obstetrician rather than a surgeon who made the connection between antisepsis and death rates among patients. Hungarian physician Ignaz Philipp Semmelweis (1818–1865) noticed that the death rate in the maternity ward was much higher among women cared for by doctors than by midwives. His investigation led him to recognize that doctors often went directly from performing autopsies (procedures in which midwives had no role) to delivering babies. In 1846 Semmelweis implemented procedures for doctors to wash their hands with chlorinated lime before examining obstetrical patients, and maternal death rates from childbirth FEVER (puerperal fever) plummeted.

It was 20 years later that Louis Pasteur (1822–1895) and Joseph Lister (1827–1912) proved the connection between microscopic "germs" and illnesses such as infection, and by the 1870s antisepsis was the standard of practice not only for childbirth but also for surgery and other treatment modalities. Today surgeons and other

members of the surgical team follow stringent HAND WASHING (scrubbing) procedures, and wear sterile gowns and gloves in the operating room. The widespread use of ANTIBIOTIC MEDICATIONS has further reduced the risk for postoperative infection.

THE SURGERY TEAM

A typical surgery team today includes the

- primary surgeon
- assisting surgeon or physician assistant; may be several depending on the type of operation
- scrub nurse or surgery technician (also called surgical technologist)
- circulating nurse
- anesthesiologist or certified nurse anesthetist
- perfusionist for certain surgeries

Breakthrough Research and Surgical Advances

The last half of the 20th century saw surgery surge to the forefront of treatment options for numerous health conditions, revolutionizing care as well as survival for heart disease, cancer, CONGENITAL ANOMALY, and major trauma. OPEN HEART SURGERY and ORGAN TRANSPLANTATION are now conventional treatment options. Among the most exciting advances in surgery in recent years has been the evolution of MINIMALLY INVASIVE SURGERY, operations that use tiny video cameras to display the operative site on a monitor similar to a television screen. The surgeon operates using the display for visual guidance, much like a sophisticated video game. Through small incisions, called ports, the surgeon inserts tiny instruments. Minimally invasive surgery reduces the need for large, open incisions, decreasing patient discomfort and recovery time. Operations that were once major ordeals have become fairly minor procedures. Surgeons look forward to a future in which minimally invasive surgery becomes the standard for nearly all kinds of operations.

A–E

ambulatory surgery Surgery, sometimes called same-day or outpatient surgery, in which the person comes to the hospital or AMBULATORY SURGERY FACILITY the day of the surgery, has the OPERATION, and goes home without an overnight stay in the hospital. Often the operation uses MINIMALLY INVASIVE SURGERY procedures such as endoscopic methods (laparoscopy, arthroscopy), which greatly reduce the size of the incision and the amount of trauma the body experiences during operation. Minimally invasive surgery techniques allow a rapid course of recovery in the immediate postoperative period as well as over the longer term. Surgeons also can perform numerous OPEN SURGERY procedures on an ambulatory surgery basis. People tend to feel more comfortable recovering in their own homes and often require lower doses of PAIN medications during their recovery. As well, a shorter stay reduces the risk for NOSOCOMIAL INFECTIONS (infections acquired from exposure to BACTERIA in the hospital environment) and more quickly returns a person to regular activities.

Because each person's rate of recovery is unique, some people more quickly return to CONSCIOUSNESS from sedation or general ANESTHESIA and to function from regional anesthesia to engage in basic activities such as drinking fluids and going to the bathroom. Underlying health conditions also influence how quickly a person is ready to leave after ambulatory surgery. Hospitals and ambulatory (outpatient) surgery facilities are equipped and staffed to handle medical emergencies that may arise and are prepared for a person to stay overnight in a hospital should circumstances warrant additional care or observation. The person returns to his or her surgeon for follow-up care such as wound check, suture removal, and dressing changes.

See also ANALGESIC MEDICATIONS; ENDOSCOPY; LASER SURGERY; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT; WOUND CARE.

anesthesia The intentional establishment of loss of PAIN sensation or of consciousness to make a surgical OPERATION possible. Anesthesia may be local, regional, or general, depending on the operation and on the individual's health circumstances and preferences. Doctors sometimes use local and regional forms of anesthesia to treat severe or CHRONIC PAIN not related to surgery.

Anesthesia today is very effective as well as safe. There are several types of anesthesia and numerous anesthetic agents. The anesthesiologist or anesthetist selects the types and agents according to the operation and the person's health conditions and health status, and may combine types and agents to achieve the desired anesthetic effect. The risks of anesthesia vary with the type and agent though are generally minimal.

Individual response to anesthetic agents varies, so the anesthesiologist or anesthetist very closely monitors the person's vital signs and level of anesthesia throughout the operation. After the operation monitoring continues in the postanesthesia care unit (PACU), also called the recovery room, until the person has emerged from anesthesia enough to go to a hospital room or for discharge home (AMBULATORY SURGERY).

Local Anesthesia

Local anesthesia numbs a small area of the body for minor operations such as removal of a LIPOMA (benign tumor of fatty tissue) or NEVUS (SKIN lesion such as a mole). The surgeon generally administers local anesthesia by injection into and surrounding

the site of the operation. Local anesthetic agents block the ability of neurons (NERVE cells) to send nerve signals, preventing the perception of pain. Some local anesthetic agents contain EPINEPHRINE, a vasoconstrictor that reduces bleeding.

The effect of a local anesthetic may last from 20 minutes to 12 hours or longer, depending on the agent and the extent of infiltration of the area. Surgeons sometimes use local anesthetic to infiltrate the area of an operative site at the end of the operation to provide extended pain relief. Surgeons may combine local anesthesia and conscious sedation to reduce anxiety and improve the person's level of comfort during and after the operation. Some amount of a local anesthetic enters the BLOOD circulation and can cause sensations such as lightheadedness or a feeling that the lips are buzzing.

COMMON LOCAL AND REGIONAL ANESTHETIC AGENTS

benzocaine	bupivacaine	chloroprocaine
etidocaine	lidocain	emepivacaine
prilocaine	procaine	ropivacaine
tetracaine		

Regional Anesthesia

Regional anesthesia is an injection that infiltrates nerves to blocks pain signals from a large area of the body. An anesthesiologist or anesthetist administers regional anesthesia. The most common forms of regional anesthesia include

- regional nerve block, in which the anesthesiologist or anesthetist administers a single injection of the anesthetic agent into or around a major nerve to block sensation from the fingers, hand, arm, toes, foot, or leg
- caudal, in which the anesthesiologist or anesthetist administers a single injection of the anesthetic agent into the caudal canal in the sacrococcygeal (tailbone) region of the spine to block sensation in the pelvis and perineum
- epidural, in which the anesthesiologist or anesthetist places a thin catheter into the space surrounding the SPINAL CORD and injects the anesthetic agent, potentially as a steady flow or repeated times, to block sensation from the point of injection downward for operations on the lower abdomen and lower extremities
- spinal, in which the anesthesiologist or anesthetist administers a single injection of the anesthetic agent directly into the CEREBROSPINAL FLUID around the spinal cord to block sensation from the point of injection downward for operations on the abdomen and lower extremities

Many of the anesthetic agents are the same for regional anesthesia as for local anesthesia. As occurs with local anesthetics, a small amount of the anesthetic agent enters the blood circulation and can cause mild effects such as HEADACHE or TINNITUS (ringing in the ears). These effects generally go away within an hour. Because caudal, epidural, and spinal anesthesia affect the pelvic region and the muscles of the BLADDER, the surgeon may instruct placement of a urinary catheter until the anesthetic wears off. The surgeon may sometimes leave the epidural catheter in place for 24 to 48 hours for postoperative administration of light anesthesia or ANALGESIC MEDICATIONS for pain relief.

Regional nerve blocks, caudal anesthesia, and epidural anesthesia may take up to 20 minutes to become effective. Spinal anesthesia takes effect immediately. Though regional anesthesia blocks only the sensory nerves, movement of the anesthetized region is difficult because the lack of sensation makes the affected body parts feel heavy and uncontrollable. A person has adequately recovered from regional anesthesia when he or she can safely walk or regains preanesthesia sensation or movement of the affected area.

Complications are rare with regional anesthesia though may include prolonged labor during CHILDBIRTH, irritation or bleeding at the injection site, drop in BLOOD PRESSURE, and post-anesthesia headache (with epidural or spinal anesthesia). Infection and injury to the nerves are possible though extremely rare. Recovery from regional anesthesia is generally uneventful and fairly rapid.

Conscious Sedation

Conscious sedation alters a person's awareness of pain and activities taking place to and around him or her. With conscious sedation a person generally can answer questions, respond to instructions, and tell the doctor whether he or she is experiencing pain or discomfort though has little or no memory of the operation and events surrounding it when

full consciousness returns. Surgeons often use conscious sedation to improve a person's comfort and reduce anxiety during minor operations, usually in combination with local or regional anesthesia. Usually an anesthesiologist or anesthetist administers the sedative medication intravenously with ongoing monitoring of the person's response to the medication, level of awareness, and vital signs such as BREATHING rate, HEART RATE, and blood pressure.

Rarely, a person may experience NAUSEA or headache after conscious sedation. More rarely, a person may have distressing memories of the operation. Though a person appears to return to normal consciousness quickly, the medication may remain at a level in the blood circulation that affects perception and function for 24 hours after its administration. Doctors caution people to avoid driving or performing activities that require alertness and coordination for at least 24 hours after conscious sedation.

POTENTIAL DRUG INTERACTIONS WITH ANESTHESIA

Many prescription medications, OVER-THE-COUNTER (OTC) DRUGS, NUTRITIONAL SUPPLEMENTS, and MEDICINAL HERBS AND BOTANICALS can interfere with anesthesia or BLOOD clotting. It is important to tell the surgeon of all such medications and products. The surgeon or the anesthesiologist may request the person to stop taking certain drugs or herbs for a period of time before and sometimes also after surgery.

General Anesthesia

General anesthesia establishes a state of deep UNCONSCIOUSNESS in which the anesthetic agents circulate in the body to block pain signals, prevent movement, and block memory of the operation. The anesthetic agents may be gases the person inhales or medications (such as sedatives, hypnotics, and MUSCLE relaxants) the anesthetist or anesthesiologist injects intravenously. An endotracheal tube inserted through the MOUTH, into the THROAT, and to the top of the trachea allows the anesthesiologist to seal the airway to prevent foreign matter from entering the LUNGS, as the anesthetic suppresses the COUGH REFLEX that would normally keep mucus and debris from entering the trachea. The endotracheal tube also ensures that oxygen and anesthetic gases directly enter the lungs. General anesthesia is the standard for operations on the upper abdomen and chest as well as for many major orthopedic operations. In some circumstances the anesthesiologist may combine epidural or spinal anesthesia with general anesthesia. Many general anesthesia agents are fast acting and short lived, allowing rapid anesthetic induction as well as quick recovery.

COMMON GENERAL ANESTHETIC AGENTS

Inhaled		
enflurane	halothane	isoflurane
methoxyflurane	nitrous oxide	
Injected		
etomidate	KETAMINE	methohexital
propofol	thiopental	

Sophisticated equipment allows precise and safe administration of inhaled anesthetics, including ongoing adjustments of carbon dioxide and oxygen concentrations. The anesthesiologist or anesthetist continuously monitors the person's vital signs, including breathing rate, oxygen saturation, heart rate, blood pressure, and body temperature. The most common side effects of general anesthesia are nausea, VOMITING, a slow return to normal bowel activity, and a prolonged sense of grogginess. The anesthesiologist or anesthetist can administer medications to ease or relieve these symptoms. Sore throat is a common complaint after general anesthesia, a consequence of the endotracheal tube.

Though most general anesthetic agents do not persist in the body at functional levels beyond 24 to 36 hours, many people feel they are not quite themselves for several days after general anesthesia. Postoperative analgesic medications can exacerbate this perception. Walking, to the extent possible, and stool softeners help BOWEL MOVEMENT return to normal. Allergic reaction to anesthetic agents is uncommon but occurs, so it is important to tell both the surgeon and the anesthesiologist or anesthetist of any allergies, including to foods. Smoking, certain prescription medications, ILLICIT DRUG USE, and ALCOHOL consumption affect the ways in which various anesthetic agents function in the body.

It is important to avoid driving or engaging in activities that require focused attention (including making important decisions and signing legal documents) until it is clear that the effects of general anesthesia have completely worn off.

A rare but potentially life-threatening complication of general anesthesia is malignant hyperthermia, in which the person's body temperature rises rapidly and high, muscles become rigid or SPASM, and heart rate and blood pressure vacillate wildly and widely. Doctors believe malignant hyperthermia has a genetic foundation because it occurs in families, though the precise genetic involvement remains unknown. Death as a complication of general anesthesia, though possible, is very rare. Continued advances in anesthetic agents and administration techniques are improving the experience and safety of general anesthesia.

See also NEURON; POSTOPERATIVE PROCEDURES; PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT; WOUND CARE.

blood autodonation A practice in which a person donates his or her own BLOOD for potential self-use during a major OPERATION or health emergency such as major trauma. The hospital or blood bank stores the blood for specific and sole use by the person. The person may authorize the hospital or blood bank to release the blood for general use as components (such as ALBUMIN and PLASMA) if he or she does not require it, though guidelines vary according to the procedures in place for collecting autodonated blood. Testing procedures for autodonated may be less stringent than for general BLOOD DONATION because only the donor will receive the blood.

Most people who choose autodonation do so out of concern about the potential for INFECTION such as HEPATITIS acquired from general donation blood. Though screening procedures and tests make the blood supply as safe as possible, the risk of such infection remains a possibility. Autodonation also eliminates the risk for transfusion reaction, which may occur when donor blood carries antibodies that activate an IMMUNE RESPONSE in the recipient. Pretransfusion testing can detect most but not all of these scenarios. Autodonation also ensures the availability of blood for people who have uncommon blood types.

See also ANTIBODY; BLOOD TRANSFUSION; BLOOD TYPE.

bloodless surgery Specialized techniques that allow surgeons to perform major operations to avoid the need for BLOOD TRANSFUSION. Many people oppose BLOOD transfusion on the basis of religious beliefs and others because they have concerns about the safety of donated blood. Though stringent screening and testing procedures for donated blood have minimized the risk of acquired INFECTION from the US blood supply, a slight risk of this remains for whole blood and certain blood products.

Performing surgery when blood transfusion is not an option requires careful planning. When the OPERATION is elective (nonemergency) the person can prepare by taking medications such as ERYTHROPOIETIN (EPO) to boost his or her ERYTHROCYTE (red blood cell) production and donating his or her own blood in advance of the surgery for use if a transfusion becomes necessary. Having more erythrocytes means the blood can carry more oxygen, which encourages HEALING. It also allows the surgeon to administer intravenous fluids during surgery to maintain adequate fluid volume without concern for diluting the blood to the extent that ANEMIA develops.

During the operation, whether elective or emergency, the surgeon can use methods to collect any blood the person loses, filter it, and return it to the person instead of transfusing donor blood. Surgeons also use precision techniques that minimize blood loss when they perform bloodless operations. Sometimes these techniques are time consuming, which makes the surgery more expensive. However, many of the surgical techniques surgeons use for bloodless surgery have become standard for all operations of the same type because they reduce the risk for postoperative infection and encourage more rapid healing and recovery.

Emergency bloodless surgery can be more of a challenge, particularly when there are bleeding injuries that deplete the blood supply even before

surgery begins. Fluid expanders sometimes can maintain the body's fluid level without impairing the blood's ability to carry oxygen. Bloodless surgery techniques and blood recycling become essential when the operation is an emergency.

See also BLOOD AUTODONATION; SPIRITUAL BELIEFS AND HEALTH CARE.

endoscopic surgery See MINIMALLY INVASIVE SURGERY.

L–M

Langer's lines The natural linear pathways, also called cleavages, of the fasciae fibers (connective tissue layer beneath the SKIN that covers the muscles) throughout the body. Langer's lines resemble a topographic map when overlaid on an outline of the human body. Each person has a unique configuration of Langer's lines, though general patterns are common across individuals. Alignment with relevant Langer's lines is one of several factors a surgeon considers when planning an OPERATION's incision. Surgical incisions that parallel Langer's lines tend to require less suturing and to heal with less obvious scarring than incisions that run counter, and particularly perpendicular, to Langer's lines. Wounds from cuts or punctures are often more severe when they occur in opposition to Langer's lines, tending to gape and tear more than wounds that parallel Langer's lines. The RASH or eruptions of some skin conditions, such as PITYRIASIS rosea, follow Langer's lines.

See also DERMATOME.

laparoscopic surgery See MINIMALLY INVASIVE SURGERY.

laser surgery Any OPERATION in which the surgeon uses a device that focuses high-intensity lightwaves that generate heat to cut or ablate (destroy) tissue. *Laser* is an acronym for "light amplification by stimulated emission of radiation." Lasers came into common use in medicine and surgery in the 1960s; the first applications were for the repair of detached RETINA.

The lightwave emission of a laser differs from ordinary light because it is

- all one wavelength (monochromatic)
- organized and unified
- directional and concentrated

There are different types of lasers, classified according to the mechanism by which they produce lightwaves, the length of the lightwaves, and the pattern of emission (continuous or pulsed). The different wavelengths and pulse patterns of emitted light permit targeted use of lasers from making incisions (cutting) to treating discolorations of the SKIN such as a port wine stain BIRTHMARK. The laser's lightwave determines what tissues will absorb the light and what tissues will allow the light to pass through them. For example, the BLOOD in blood vessels absorbs the yellow light of the pulsed laser, though the pigment of light-colored skin does not. Most lasers emit lightwaves in the infrared spectrum; the "cool" lasers emit lightwaves in the ultraviolet spectrum.

Laser lightwaves, like other lightwaves, can travel via fiberoptics, allowing the surgeon to direct the laser emission to a specific location, even one that is deep within the body. Laser surgery requires the surgeon to complete specialized training and requires specialized equipment and facilities for safe use.

Surgical lasers have increased options in all areas of surgery but have revolutionized two areas of treatment in particular: ophthalmologic (EYE) surgery and dermatologic (skin) surgery. The surgeon can so precisely focus and target the laser's beam that any incidental damage to surrounding tissue is nearly nonexistent. Laser surgery incisions tend to heal with minimal scarring. The heat the laser generates kills BACTERIA on the skin at the incision site, reducing the risk for postoperative INFECTION. As well, the intense heat instantly seals blood vessels to reduce bleeding at the site of the incision, making the surgical laser the instrument

TYPES OF SURGICAL LASERS

Laser Type	Characteristics	Surgical Application
argon gas	shallow penetration moderately hot only pigmented tissues and fluids absorb the lightwaves	dermatologic procedures refractive surgery (vision correction) coagulate bleeding BLOOD vessels
carbon dioxide (CO_2)	shallow penetration very hot only pigmented fluids absorb the lightwaves	instead of scalpel for incisions vaporize tissue (including tumors) dermatologic procedures such as SKIN resurfacing
neodymium:yttrium-aluminum garnet (Nd:YAG)	deep penetration moderately hot all fluids in the body absorb the lightwaves	fiberoptic transfer to locations within the body vaporize or shrink tumors remove pigmented lesions remove tattoos
pulsed dye	shallow penetration moderately hot tunable wavelength	port wine stain and other vascular birthmarks

of choice for BLOODLESS SURGERY as well as for treating vascular disorders of the skin such as birthmarks.

Because the intense light the laser generates can burn the RETINA and cause permanent blindness, people undergoing laser surgery as well as the surgeon and other members of the surgical team must wear EYE protection when the laser is in use.

Laser surgery has the same risks as conventional surgery for bleeding and infection, and carries additional risk for BURNS and related damage. A laser can permanently discolor the skin, particularly the skin of people of color (notably African Americans, Asian Americans, and Hispanic Americans). Lasers may also cause burns of the skin. Though laser surgery makes many operations easier and more comfortable, it is important to choose a surgeon who is qualified to perform laser surgery and to fully understand the potential benefits and risks of laser surgery compared to conventional surgery.

See also LASER SKIN RESURFACING; MINIMALLY INVASIVE SURGERY; OPEN SURGERY; PHOTOTHERAPEUTIC KERATECTOMY (PTK); REFRACTIVE SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT; TATTOOS.

minimally invasive surgery Any OPERATION in which the surgeon uses an endoscope and specialized instruments to enter the body through small incisions, called ports. An endoscope is a lighted, flexible tube with a tiny camera at the tip that sends visual images of the operative site to a monitor similar to a television screen. The endoscope is specialized for the procedure, such as a laparoscope for operations within the abdominal cavity.

The surgeon watches the images on the screen rather than seeing the operative site directly. Minimally invasive surgery is in contrast to OPEN SURGERY, in which the surgeon makes an incision large enough to allow direct access to the operative site. Surgeons must receive specific training in the minimally invasive procedures they perform, which require special equipment and instruments. Surgeons sometimes combine minimally invasive procedures with LASER SURGERY, assisted open surgery, or other operative techniques.

Recovery time is typically faster and less painful than with open surgery as there is less intrusion into the body. Many minimally invasive surgery operations are ambulatory surgeries that do not require an overnight stay in the hospital. As is the case with any surgery, minimally invasive procedures carry some risk for ANESTHESIA complications, bleeding, and INFECTION.

See also AMBULATORY SURGERY; ENDOSCOPY; SURGERY BENEFIT AND RISK ASSESSMENT.

open surgery Any surgical OPERATION in which the surgeon makes an incision that allows direct access to the operative site. An open surgery incision may be quite large. Until the emergence of MINIMALLY INVASIVE SURGERY procedures in the 1980s open surgery was the standard of surgical treatment for nearly all operations. Surgeons today can perform many operations with minimally invasive techniques, reserving open surgery for circumstances in which the surgeon needs the broad exposure open surgery provides. Such circumstances include OPEN HEART SURGERY for operations such as CORONARY ARTERY BYPASS GRAFT (CABG) and heart valve replacement, open THORACOTOMY for operations on the LUNGS, open laparotomy for major operations on the structures of the abdomen such as the GALLBLADDER and intestines, and ORGAN TRANSPLANTATION. Common risks of any surgery include bleeding and INFECTION, which are somewhat more likely with open surgery than with minimally invasive surgery. As well, recovery and recuperation take longer with open surgery, generally 4 to 12 weeks, depending on the type of operation. Open surgery may also leave a more noticeable SCAR after HEALING.

See also ANESTHESIA; LASER SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT.

operation A surgical procedure to enter the body and conduct a repair, remove a tumor, or in some other way alter a structure or organ. A surgical operation takes place under sterile conditions in a controlled environment, an operating room, used exclusively for surgery. Minor operations may take place in AMBULATORY SURGERY centers and specialized surgical clinics; major operations take place in hospitals that have sophisticated facilities and experienced staff to provide care before, during, and after surgery. Though traditionally the term *surgery* has applied to the medical specialty of

COMMON SURGICAL OPERATIONS

Surgical Operation	Purpose
adenoidectomy	remove chronically infected and enlarged adenoids
APPENDECTOMY	remove an inflamed or infected APPENDIX
ATHERECTOMY	remove ATHEROSCLEROTIC PLAQUE deposits from within arteries
BLEPHAROPLASTY	repair or reconstruction of the eyelids
CHOLECYSTECTOMY	remove the GALLBLADDER
colectomy	remove part or all of the COLON
COLOSTOMY	create a passage from colon through the abdominal wall

Surgical Operation	Purpose
craniotomy	operations on the BRAIN and related structures, PITUITARY GLAND
cystectomy	remove the urinary BLADDER
ENDARTERECTOMY	remove an occlusion from an ARTERY
EPISIOTOMY	incision to widen the vaginal opening during CHILDBIRTH
GASTRECTOMY	remove part or all of the STOMACH
hernioplasty	repair of a HERNIA
HYSTERECTOMY	remove the UTERUS
LAMINECTOMY	remove a vertebral disk
laparotomy	operations on structures of the abdomen such as the intestines, LIVER, appendix, uterus, OVARIES, FALLOPIAN TUBES
LARYNGECTOMY	remove the larynx
lobectomy	remove a lobe of the LUNGS
MASTECTOMY	remove a BREAST
NEPHRECTOMY	remove a kidney
nephrotomy	remove a tumor or remove kidney stones
OOPHORECTOMY	remove ovaries
ORCHIECTOMY	remove a testicle
OTOPLASTY	repair or reconstruction of the outer EAR
pneumonectomy	remove an entire lung
PROSTATECTOMY	remove the PROSTATE GLAND
resection	remove (excise) a portion of a structure
RHINOPLASTY	repair or reconstruction of the NOSE
RHYTIDOPLASTY	repair or reconstruction of the face (facelift)
salpingectomy	remove a fallopian tube
SPLENECTOMY	remove the SPLEEN

Surgical Operation	Purpose
THORACOTOMY	operations on structures within the chest except the HEART
tonsillectomy	remove chronically infected and enlarged tonsils
TRACHEOSTOMY	create a passage from the TRACHEA through the surface of the neck
TYMPANOPLASTY	repair or reconstruction of the TYMPANIC MEMBRANE (eardrum)
VASECTOMY	remove a segment of the VAS DEFERENS

surgery, many people now use the terms *operation* and *surgery* interchangeably.

See also ARTHROSCOPY; BARIATRIC SURGERY; CARDIAC CATHETERIZATION; CATARACT EXTRACTION AND LENS REPLACEMENT; CESAREAN SECTION; ENDOSCOPY; JOINT REPLACEMENT; LASER SURGERY; MINIMALLY INVASIVE SURGERY; MOHS' SURGERY; PLASTIC SURGERY; REFRACTIVE SURGERY; SURGERY BENEFIT AND RISK ASSESSMENT; TUBAL LIGATION.

organ transplantation The surgical replacement of a nonfunctioning vital organ with a functional organ acquired from a donor. Most donor organs are allogeneic, also called deceased donation or cadaver donation, in which a specialized surgical team removes the donated organs after a person's death when the person has previously authorized, or when the person's family authorizes at the time of the person's death, organ donation. In some circumstances a person may make a living organ donation to another person, such as for kidney, lung lobe, and partial LIVER. US surgeons perform almost 27,000 organ transplantations each year, nearly 7,000 of which are organs from living donors. The most commonly transplanted organs are KIDNEYS and livers. However, approximately 89,000 people remain on waiting lists for donor organs.

TRANSPLANTED ORGANS AND TISSUES

BONE MARROW	CORNEA	HEART
ISLETS OF LANGERHANS cells	kidney	LIVER
lung	PANCREAS	SKIN
SMALL INTESTINE	stem cells	

Organ Allocation and Acquisition

Organ transplantation transitioned from experimental to mainstream in the 1980s, riding a wave of technologic advances and the success of cyclosporine, the first effective immunosuppressive DRUG. In 1984 the US Congress passed the National Organ Transplant Act (NOTA), which established the Organ Procurement and Transplantation Network (OPTN) to ensure consistency and equity in the allocation of deceased donor organs. OPTN is a not-for-profit organization that is a collaborative union of public and private organizations. The United Network for Organ Sharing (UNOS) administers OPTN under contract to the US Department of Health and Human Services. Hospital transplant programs across the United States determine a person's eligibility for transplantation, then submit the person's name and health data (such as organ needed and blood type) to the UNOS database.

A regional organ procurement organization (OPO) receives notification from hospitals and other health-care providers when deceased donor organs become available within its geographic boundaries. The OPO coordinates the effort to match the organs with appropriate donors, initiating a "match run" from the UNOS database. The match run identifies prospective transplant recipients waiting for the particular kind of organ, the medical urgency of the transplant need, the general health circumstances, and the geographic proximity of the donor organ to the prospective recipient. The matched names go on a list for the organ, ranked in order of need. UNOS generates a new match run each time an organ becomes

available, specific for each kind of organ, so a waiting recipient may appear on several lists and in different rankings relative to others on the same list.

The available organ goes to the waiting recipient who is the best match on as many criteria as possible. For organs such as the HEART and LUNGS, geographic proximity is a critical factor because the window of opportunity for transplantation is so short. Body size may be important for organs such as the liver, heart, and lungs. Typically gender and ethnicity or race are not factors for vascularized organ transplants unless they influence body size. Financial status is not a consideration under any circumstances. Living donor transplants are not subject to OPTN/UNOS procedures but rather are coordinated privately between the donor and the recipient.

Organ Transplantation Surgery

Transplantation of vascularized (solid) organs is major surgery that may require the organ recipient to be prepared for surgery within hours of notification that an organ is available. Time is especially critical for heart, lung, and heart–lung transplantation. In most transplant operations the surgeon transplants a single organ. Combination transplantations are becoming more common, however, with surgeons transplanting together heart and lung, SMALL INTESTINE and liver, or kidney and pancreas. The operation to transplant a single organ may take three to five hours; combination transplants may take longer. The transplant recipient may remain hospitalized for several weeks after surgery, depending on the organ, rate of recovery, and overall health status.

With some organs, such as kidneys, the surgeon can leave the native organ in place and transplant the donor organ in an adjacent location. This is a heterotopic transplant. The surgeon may also choose to remove the recipient's native, diseased organ and transplant the donor organ in its place, such as the liver. This is an orthotopic transplant. One approach is not necessarily easier or more effective than the other for either the surgeon or the recipient. Circumstances that shape the decision include the recipient's general health status, anatomic characteristics, and the organ being transplanted.

Life after Transplantation

The course of recovery after transplantation varies with the organ transplanted, age, and overall health circumstances. Most organ transplant recipients are able to return to previous work, recreational, and lifestyle activities they enjoyed before experiencing the health circumstances that made their transplants necessary, usually within two to three months. Transplant recipients do require ongoing medical assessment and care, which may consist of doctor visits every few weeks for the first 6 to 12 months after the transplant and every 6 to 12 months indefinitely, depending on the organ transplanted and general health status.

The key health risks after transplantation are primary organ failure and organ rejection. Primary organ failure occurs when the organ does not function after transplantation. The organ may start to function and then stop or may never begin functioning. Some organs, such as the kidneys, may take several weeks to several months to start functioning or to function normally, which is the usual course of events for them and does not necessarily indicate that the transplant has failed. It is not unheard of for a kidney transplant recipient to require renal hemodialysis after the transplant OPERATION, and hemodialysis remains a therapeutic option when a transplanted kidney does fail. Primary organ failure of the heart, lungs, or liver is a medical emergency that requires retransplantation as soon as possible. Numerous and often collusive factors may account for primary organ failure of a transplant.

Organ rejection occurs when the recipient's IMMUNE SYSTEM produces antibodies that attack the transplanted organ and is a process rather than an event. Every transplant experiences rejection to some degree because rejection represents the body's natural IMMUNE RESPONSE. Organ rejection may be acute or chronic. Acute rejection develops rapidly and may present symptoms similar to a viral INFECTION such as the flu, though often there is tenderness or PAIN at the site of the transplant. Acute rejection requires immediate medical treatment with immunosuppressive agents to attempt to subdue the immune response and minimize damage to the organ. Episodes of acute rejection are common in the first year after transplantation and can occur months to years later. A single

episode of acute rejection is seldom enough to cause organ failure, especially when treatment is prompt.

IMMUNOSUPPRESSIVE AGENTS TO MINIMIZE ORGAN REJECTION

Induction and Antirejection (up to 30 days)	
Atgam	basiliximab
daclizumab	methylprednisolone
muromonab CD3	rapamycin
Thymoglobulin	
Maintenance (long-term)	
azathioprine	cyclosporine
mycophenolate mofetil	prednisone
rapamycin	tacrolimus

Chronic organ rejection represents the steady and slow consequences of the immune system's efforts to eliminate the organ, which the immune system perceives as an "intruder." At present the standard of treatment to minimize organ rejection is lifelong IMMUNOSUPPRESSIVE THERAPY, taking drugs that suppress the immune response. Doctors monitor immune status and transplanted organ function with regular BLOOD tests. The risks of long-term immunosuppression include increased vulnerability to infection (such as COLDS, flu, and OPPORTUNISTIC INFECTIONS), which may require ANTIBIOTIC PROPHYLAXIS or ANTIFUNGAL MEDICATIONS. Long-term immunosuppression also increases the risk for lymphoma and MULTIPLE MYELOMA, two cancers of the immune system; when detected early these cancers are easily treatable. Immunosuppressive agents also have numerous drug interactions and potential side effects.

Organ Donation

Nearly anyone can be an organ donor. Most US states incorporate organ donation permission on driver's licenses. A driver's license is the most common form of identification Americans carry, and MOTOR VEHICLE ACCIDENTS are the most common cause of unexpected death. As well, organ donation authorization forms are available at hospitals, medical centers, doctor's offices, public health departments, and other providers of health-care services. Some states also have donor registries. A person age 18 or older can authorize organ donation for himself or herself; a parent or legal guardian must authorize organ donation for a person under the age of 18. It is also a good idea for a person who desires to donate his or her organs after death to let a close relative or friend know of this intention. Such knowledge eases the decision-making process family members may face.

Doctors must follow accepted standards of practice for determining when BRAIN DEATH (irreversible loss of complete BRAIN function) has occurred or the person is pronounced dead, after which they may seek the family's permission to proceed. The removal of donated organs, called organ retrieval or organ harvesting, takes place in an operating room under sterile conditions. The window of opportunity for transplanting a donated organ ranges from 4 hours after harvesting for a heart, 6 hours for lungs, 12 hours for liver, and to up to 24 hours for a kidney. Special preservative solutions and methods (such as pulsatile perfusion, which moves chilled preservative fluid through the organ) help keep organs viable until transplantation.

NO COST FOR DONOR ORGANS AND TISSUES

Federal law in the United States prohibits buying and selling human organs and tissues. Organs and tissues for transplantation must come from donors. The expenses associated with organ transplantation are those of medical care before and after the transplantation and for the transplant operation and its related costs (such as for hospitalization). There is no cost for being on the organ donor registry or for donor organs and tissues.

Surgeons carefully remove organs to preserve them as intactly as possible. Harvesting of hearts and lungs must be take place before the heart stops, which requires certification of brain death and often life support to maintain oxygenation and BLOOD circulation until the organ retrieval team can remove them. When doctors cannot use the entire organ, they sometimes can make use of key parts. For example, a heart that has significant myocardial damage due to HEART ATTACK may have healthy valves, which doctors can harvest for heart valve replacement. There is no cost to the person's family

for harvesting donated organs, nor is there disfiguration of the donor's body. Under US medical confidentiality laws, the donor remains anonymous to the recipient and the recipient remains anonymous to the donor's family.

Availability of donor organs remains the most significant challenge for organ transplantation, which has become the standard of care for END-STAGE RENAL DISEASE (ESRD), end-stage HEART FAILURE, and end-stage LIVER FAILURE. The need for donor organs is about four times greater than the availability. The US government maintains a Web site (www.organdonor.gov) to provide information updates about organ donation and a downloadable organ donor card. Another Web site (www.transplantliving.org) provides comprehensive information from OPTN/UNOS about the entire organ transplantation process, from eligibility for transplantation to life after receiving a transplant.

See also ANESTHESIA; BLOOD TRANSFUSION; CIRRHOSIS; EPSTEIN-BARR VIRUS; GRAFT VERSUS HOST DISEASE; HEART TRANSPLANTATION; ISLET CELL TRANSPLANTATION; KIDNEY TRANSPLANTATION; LIVER TRANSPLANTATION; LUNG TRANSPLANTATION; SKIN REPLACEMENT; SURGERY BENEFIT AND RISK ASSESSMENT.

P

patient controlled analgesia (PCA) The postoperative self-administration of intravenous (IV) PAIN relief (analgesic) medication. PCA requires an IV (a thin catheter inserted into a VEIN), a PCA pump that contains a special syringe with the pain medication, and a PCA control button. Each time the person depresses the PCA button the PCA pump releases a certain amount of pain medication from the syringe into the IV. Most people feel pain relief within a few minutes of pressing the button.

The PCA pump can release medication only according to the amount and frequency for which it is programmed, no matter how often the person presses the button, so there is no danger of receiving too much. An alarm on the PCA pump notifies nursing staff when the amount of medication in the syringe gets low or when there is any disruption of the pump's proper function. The PCA pump may also be programmed to deliver a steady flow of pain relief medication, with extra medication released with the button as the person needs it to maintain comfort.

Numerous studies show that people tend to have less anxiety about postoperative pain and pain relief and use less pain relief medication with PCA. As well, appropriate pain control facilitates faster HEALING. Within a few days after an OPERATION most people are able to switch to oral (by MOUTH) pain medications.

See also ANALGESIC MEDICATIONS; SURGERY BENEFIT AND RISK ASSESSMENT.

plastic surgery Any surgical OPERATION to alter the appearance of a body area or part. Plastic surgery may be reconstructive (re-creates or repairs a body part that is damaged or missing) or cosmetic (changes physical appearance for reasons of personal preference). Though both disciplines encompass elective operations, the US health-care system considers reconstructive surgery to be medically necessary; therefore, health insurance plans typically pay for reconstructive operations. Cosmetic surgery operations are not medically necessary and health insurance plans seldom pay for them.

In some circumstances the nature of a plastic surgery operation overlaps between cosmetic and reconstructive. For example, a person may desire RHINOPLASTY (NOSE alteration) because of dissatisfaction with the nose's appearance, though the surgeon's examination leads to the discovery that the person also has a deviated septum, which affects BREATHING and the health of the SINUSES. A person may seek plastic surgery to alter the perception of aging that arises from drooping eyelids, and then discover the eyelids obscure the field of vision.

Reconstructive Surgery

Reconstructive surgery rebuilds missing or lost structures with the goal to restore function. The loss may be due to numerous factors that include CONGENITAL ANOMALY, traumatic injury, BURNS, disease processes, and surgical treatment for conditions such as cancer. Reconstructive surgery is often complex and requires multiple operations to achieve the desired result. Reconstructive operations performed in childhood may need revision as the child grows. Reconstructive surgeons may coordinate care and treatment with surgeons and physicians in other specialties such as orthopedics (bones and connective tissues) and neurology (nerves). Doctors often request a plastic surgeon to suture or otherwise repair LACERATIONS and wounds to the face or hands. Plastic surgeons perform about five million operations a year in the United States.

MOST COMMON RECONSTRUCTIVE OPERATIONS

BREAST reconstruction	CONGENITAL ANOMALY reconstruction
laceration repair	operations on the hands and fingers
SCAR revision	tumor removal

Cosmetic Surgery

Cosmetic surgery alters appearance for aesthetic reasons and can have profound psychological and emotional benefits. US plastic surgeons perform more than nine million cosmetic surgery procedures a year, with Americans spending more than $8 billion to have them performed. Surveys suggest people who undergo cosmetic surgery are generally satisfied with the results, perceiving improvements in self-image and social interactions. Realistic expectations are especially important when making cosmetic surgery decisions. Some cosmetic operations, such as RHYTIDOPLASTY (facelift), have long-lasting though not permanent effects because the SKIN and connective tissues continue to undergo natural changes with aging.

MOST COMMON COSMETIC OPERATIONS

abdominoplasty	augmentation mammoplasty
BLEPHAROPLASTY	body contouring after significant weight loss
liposuction	
RHYTIDOPLASTY	

Plastic Surgery Benefits and Risks

The benefits of plastic surgery often encompass improved function, appearance, and self-image or self-esteem. Specific benefits vary with the operation and often are not entirely apparent for weeks to months after the operation when HEALING is complete. As with all operations, plastic surgery operations entail risk. General risks include excessive bleeding during or after surgery, postoperative wound INFECTION, PNEUMONIA (a complication of general ANESTHESIA), unpredictable SCAR formation, and unsatisfactory or unexpected results. Death during or as a complication of plastic surgery is very rare though can occur. Cigarette smoking, DIABETES, and PERIPHERAL VASCULAR DISEASE (PVD) can limit peripheral BLOOD circulation, slowing healing and increasing the risk for complications.

It is not possible for the surgeon to guarantee the outcome of a plastic surgery operation. People sometimes have unrealistic expectations for what the operation can achieve, leading to dissatisfaction with the results. It is crucial to thoroughly understand what the operation can and cannot accomplish and the full spectrum of potential complications and risks; it is equally important to select a qualified (board-certified) plastic surgeon who is experienced in performing the desired operation and who performs surgeries in an appropriately credentialed and licensed facility.

PLASTIC SURGERY OPERATIONS

abdominoplasty	augmentation mammoplasty
BIRTHMARK removal or reduction	BLEPHAROPLASTY
brachioplasty	body contouring
brow lift	BREAST reconstruction
facial implants	cervicoplasty
laceration repair	HAIR transplantation
lip augmentation	LASER SKIN RESURFACING
liposuction	lipoplasty
mentoplasty	mastopexy
panniculectomy	OTOPLASTY
POLYDACTYLY correction and reconstruction	platysmaplasty
RHYTIDOPLASTY	reduction mammoplasty
sclerotherapy	RHINOPLASTY
SYNDACTYLY release	SCAR revision
	SKIN graft
	tissue flap surgery

See also BARIATRIC SURGERY; BOTULINUM THERAPY; CHEMICAL PEEL; DERMABRASION; HAIR TRANSPLANTATION; LASER SURGERY; SMOKING CESSATION; SURGERY BENEFIT AND RISK ASSESSMENT; WOUND CARE.

postoperative procedures The events that take place to guide a person's safe and comfortable recovery from ANESTHESIA and to initiate effective PAIN relief after a surgical OPERATION. When the operation is over the person goes to a postanesthesia care unit (PACU) where staff monitor vital signs (HEART RATE, BREATHING rate, BLOOD PRESSURE, and body temperature) and emergence from anesthesia. A person who has had regional or general anesthesia may remain in the PACU for two to four hours, until he or she regains the ability to use the anesthetized region of the body or regains CONSCIOUSNESS.

It is common and normal to feel disoriented when first coming out of anesthesia. Many people who have had general anesthesia do not realize the operation is over. It is also normal to feel

chilled and to experience discomfort, numbness, or pain. The surgeon may infiltrate the operative site with a local anesthetic to provide localized pain relief for 12 to 24 hours after the operation or place tiny catheters in the surgical wound to instill a continuous irrigation of a local anesthetic for extended pain relief. Most often the person is already receiving analgesic medications to relieve pain and generally receives PATIENT CONTROLLED ANALGESIA (PCA) during the recovery period. When fully stable the person may go to a room in the hospital, if an overnight stay in the hospital is necessary, or home to recover and recuperate. Before discharge the PACU staff provide instructions for WOUND CARE, pain management, possible complications such as unusual bleeding, and follow-up appointments with the surgeon.

See also PREOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

preoperative procedures The events that take place to prepare a person for a surgical OPERATION. Preoperative procedures for elective (nonemergency) operations may begin several days to a week before the scheduled surgery with activities such as

- preoperative consultation with the surgeon or a member of the surgeon's staff to discuss the preparations for surgery, including any revisions to routine medications, dietary restrictions, LAXATIVES or ENEMA, or SKIN-cleansing procedures as well as expectations for the operation's outcome and the anticipated recovery period
- signing of informed consent documents that specify, in detail, the planned operation and the reasons for it, the scope of surgery the surgeon may perform, and the operation's possible complications and risks
- routine BLOOD tests to assess blood cell counts, HEMOGLOBIN level, COAGULATION (clotting) times, LIVER function, and kidney function
- possible chest X-RAY, ELECTROCARDIOGRAM (ECG), and other diagnostic testing, depending on the operation and the person's health status and age
- consultation with the anesthesiologist or anesthetist to determine the optimal anesthesia choices for the person's health status and the planned operation
- health insurance preauthorization or financial arrangements

The doctor will provide instructions about not eating for a specified period of time before the scheduled operation, and about taking any daily medications on the day of the operation.

Before signing informed consent documents, it is crucial to fully understand the scope of the planned OPERATION, the expected benefits of the operation, the anticipated course of recovery, and possible complications and risks of the operation and of the ANESTHESIA.

Most people arrive at the AMBULATORY SURGERY FACILITY or hospital surgery unit several hours before the scheduled time of the operation. In preparation for the operation, a person undresses and puts on a surgical gown. The preoperative nurse starts an intravenous (IV) infusion to maintain HYDRATION and to administer medications. Surgical staff may apply electrodes to the chest to monitor HEART RATE, place a BLOOD PRESSURE cuff around the arm to monitor blood pressure, and place a PULSE oximeter over the tip a finger to monitor blood oxygenation. Some surgical facilities allow a family member or close friend to be present during these early preparations. The surgeon or assistant surgeon often visits the person before sedation or anesthesia begins to confirm the person's identity, the planned operation, and the location of the operative site (such as left leg or right BREAST). Other staff may also make these same confirmations to prevent errors. Many surgeons use a marking pen on the skin to identify the operative site. As the time for the operation to begin draws near, most people receive a sedative for relaxation and comfort.

See also POSTOPERATIVE PROCEDURES; SURGERY BENEFIT AND RISK ASSESSMENT.

S

surgery benefit and risk assessment Objective evaluation of the reasons and expectations for a surgical OPERATION. Surgery is a common therapeutic approach today, with surgeons in the United States performing more than 25 million operations a year. Risks and complications related to surgery and ANESTHESIA have declined dramatically over the past three decades, making surgery one of the safest and most effective treatments for many health conditions. However, surgery is often not the only therapeutic option for a particular condition or health circumstance. It is important to fully understand

- the specific operation the surgeon recommends and why
- the expected benefits of the operation
- other surgical operations that might also treat the problem
- the possible nonsurgical treatments for the condition
- the potential risks of the operation itself
- how the operation's risks compare to the risks of other treatment options (including nontreatment) for the condition

Some people need time to think through their options, the reasons the surgeon recommends the operation, and the possible complications of the operation. There is usually no hurry to schedule an elective operation, though symptoms such as PAIN may make the scheduling timely. It is often helpful to write down questions and concerns, then schedule an appointment with the surgeon to discuss them before making the decision to proceed with surgery.

The surgeon who will perform the operation should be qualified and experienced. Many hospitals are teaching centers where surgical residents (trained physicians who are learning advanced skills in surgery) participate in operations. They do so under the direction and close supervision of the primary surgeon. Teaching hospitals are required to obtain signed permission for staff who are in training (physicians, nurses, and ancillary staff) to participate in care delivery, including surgery. As well, for most operations the surgeon has at least one other surgeon assisting him or her. A person should know who will actually be performing the operation and the other doctors who will be assisting because these are factors that may influence the outcome of the surgery.

Surgery Benefits

The benefits of surgery are numerous and mostly specific to the planned operation. In general, surgery corrects or repairs defects, injuries, functions, or appearance. Surgery may be lifesaving, as in major trauma or CORONARY ARTERY BYPASS GRAFT (CABG), and is the first line of treatment for many forms of cancer. Surgery may also be palliative, such as to reduce pain, pressure, or other discomforts that may occur in chronic health conditions such as NEUROPATHY or terminal cancer. It is important to discuss with the surgeon the anticipated or hoped for benefits of the recommended operation.

POTENTIAL BENEFITS OF SURGERY

correct congenital defects	improved appearance
relieve intractable PAIN	improved function
treat injuries or conditions	removal of tumors

Surgery Risks

All operations have general as well as specific risks. General risks include excessive bleeding, wound INFECTION, PNEUMONIA, and death resulting from unanticipated crisis during the operation (such as HEART ATTACK or STROKE). Surgeon error is also a risk for any operation.

Personal health factors that increase surgical and anesthetic risks include cigarette smoking, ALCOHOL use, OBESITY, DIABETES, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), HYPERTENSION (high BLOOD PRESSURE), CYSTIC FIBROSIS, and CORONARY ARTERY DISEASE (CAD). Numerous medications (including herbal products, over-the-counter products, and illicit drugs) can interfere with anesthesia, BLOOD clotting, or HEALING.

Age alone does not increase risk for surgical complications. However with advancing age the likelihood of numerous health conditions increases, many of which can remain undetected until a stress such as anesthesia or surgery brings them to the forefront of the person's health picture. Such health conditions may include type 2 diabetes, ATHEROSCLEROSIS, CAD, renal (kidney) disease, LIVER disease, and sometimes hypertension.

POSSIBLE RISKS OF SURGERY

ANESTHESIA reaction	death
excessive bleeding during or after surgery	failure of the OPERATION to resolve the condition
intestinal adhesions	need for BLOOD TRANSFUSION
nerve injury	outcome other than expected
PNEUMONIA	unacceptable SCAR appearance
worsening of health condition	wound INFECTION

Second Opinion Consultation

A second opinion is an assessment from another specialist who provides treatment for the same condition for which the surgeon recommends an operation. The specialist is often another surgeon though may practice in a different subspecialty of surgery. For example, a person considering back surgery as treatment for HERNIATED NUCLEUS PULPOSUS ("ruptured disk") may have a surgery recommendation from an orthopedic surgeon and seek a second opinion from neurologist, as both specialties treat back problems. A person may also seek a second opinion from a specialist who is not a surgeon, who may recommend nonsurgical treatment options.

Because there are often numerous options for treating a particular health problem and surgery is inherently invasive (a treatment that enters the body), health experts recommend a second opinion consultation for most elective (nonemergency) operations. People sometimes worry that seeking a second opinion will offend the first surgeon in some way. However, current standards of practice support second opinions, and surgeons are themselves often the first to recommend them. Some health insurance plans require second opinion consultation for certain, and sometimes all elective, operations.

The second opinion surgeon or physician should

- be board-certified in an appropriate and relevant specialty
- practice in a different group or facility from that of the first surgeon
- know the consultation is for a second opinion

ELECTIVE OPERATIONS FOR WHICH HEALTH EXPERTS URGE A SECOND OPINION CONSULTATION

adenoidectomy	cancer operations
carpal tunnel surgery	CATARACT EXTRACTION AND LENS REPLACEMENT
CHOLECYSTECTOMY	DILATION AND CURETTAGE (D&C)
CORONARY ARTERY BYPASS GRAFT (CABG)	HERNIA repair
hemorrhoidectomy	HYSTERECTOMY
JOINT REPLACEMENT	knee surgery
MASTECTOMY	PROSTATECTOMY
tonsillectomy	vein ligation and stripping

The surgeon or physician providing the second opinion consultation will require medical records, diagnostic procedure reports, laboratory test results, and other information relevant to the condition. The doctor will conduct a thorough examination of the person, then discuss the findings and his or her professional opinions about the possible treatments. The second opinion may or may not support the initial recommendation for the operation. The person may choose which physician or surgeon will provide the recommended care. A complex health circumstance may require multiple consultations from different specialists, in

which case it may be helpful to have one's primary-care doctor assist in sorting through the options, benefits, and risks.

Informed Consent

Informed consent documents describe in detail the proposed operation, reason for the operation, recommended anesthesia options, expected benefits, and possible complications and risks. Informed consent is required before the operation may begin for all surgeries except in certain life-threatening circumstances. The informed consent documents should contain no surprises or new information; if they do, it is important to discuss the situation with the surgeon before signing them. In some circumstances the surgeon may request advance permission to perform a more extensive operation than planned, depending on the findings during the surgical operation. This permits the surgeon to do what needs to be done in a single operation rather than having the person go through a second procedure.

See also CANCER TREATMENT OPTIONS AND DECISIONS; QUALITY OF LIFE.

W

wound care The care necessary, including cleansing and dressing changes, to keep surgical incisions, or wounds, healthy as they heal. Most surgical wounds heal quickly and without complication and require very little care beyond keeping them clean and dry for one to five days after surgery. Redness at the incision line is normal, though the surgeon should evaluate any redness that extends farther than one half inch from the incision because this may indicate INFECTION. Sometimes there is bruising (ECCHYMOSIS) around the incision site, which typically heals in about a week.

By the fifth postoperative day the edges of the wound should be adhered to each other, with or without an obvious scab. Most scabs fall off 10 to 14 days after surgery, which indicates the incision is fully closed and about 85 percent healed. Factors that influence HEALING include DIABETES, cigarette smoking, and OBESITY.

Full healing is complete in three months. The SCAR may at first appear reddened and raised, though after about six months most scars are flush with the SKIN's surface and are pink or white. A scar generally continues to fade over time and remains lighter in color than the surrounding skin. Incisional scars are more sensitive than the surrounding skin to sun exposure and should be protected with SPF (sun protective factor) 30 sunscreen or clothing to prevent SUNBURN.

Skin Closures

A surgeon closes a surgical wound from the inside out, typically using fine sutures (threads that sew the tissue edges together) to bring together the layers of MUSCLE, FASCIA, and subcutaneous fat. These sutures, commonly called stitches, dissolve over 5 to 7 days as the tissues heal. The surgeon may use sutures, staples (small wires that pull together the edges of the skin), glue, or adhesive strips to close the final layer of the skin. The method of closure depends on the incision's location and length, the tension on the skin edges, and the surgeon's preference. The surgeon may use a combination of closure methods for large or abdominal incisions. The surgeon must remove staples and nondissolving sutures, typically 3 to 10 days after the OPERATION, though often recommends leaving the adhesive strips in place until they fall off on their own, usually in about 5 days. Staple or suture removal is quick and usually does not hurt, though some people find the minor pulling and tugging sensations uncomfortable or disconcerting.

Dressings and Dressing Changes

At the end of the operation the surgeon will place a surgical dressing over the incision site. The dressing is typically absorbent, as it is normal for the wound to bleed a little, and may be a pressure dressing to limit the amount of bleeding. The surgical dressing stays on for 24 hours, after which the surgeon, if the person stays overnight in the hospital, or the person may remove it. A larger incision may require replacement dressings for the next 72 hours, after which most incisions remain uncovered though some surgeons may instruct that the incision site remain covered for a longer period. When applying a fresh dressing, it is important to wash the hands with warm water and soap before touching bandages or the surgical wound. The surgeon may instruct the application of an antibiotic ointment. The surgeon will remove nondissolving skin sutures or staples 3 to 10 days after the operation, after which the incision is fairly well healed.

Postoperative Complications

Infection is the most common postoperative wound complication. Rarely a surgical wound may bleed. Though some degree of bleeding at the incision for the first 24 hours after surgery is normal for most operations, bleeding that saturates the bandage requires immediate assessment by the surgeon or hospital nursing staff. Extended irritation at the incision site (redness farther than one half inch from the incision), pus, and FEVER are early indications of infection that the surgeon needs to evaluate. Obesity, diabetes, and PERIPHERAL VASCULAR DISEASE (PVD) can affect the circulation of BLOOD in the body, particularly to the limbs. People who have these conditions should be alert to changes in the surgical wound that could suggest infection.

Discomfort or PAIN is a common and expected complication for a period of time after the operation, the severity and duration of which depends on the kind of operation. Restricting use of the operated area minimizes discomfort. The surgeon will prescribe appropriate ANALGESIC MEDICATIONS to relieve pain.

Return to Bathing or Showering and Normal Activities

Most surgical wounds are closed enough to permit showering 24 to 48 hours after surgery. Getting the incision wet does not affect the skin closures (sutures, staples, or adhesive strips). Bathing (sitting in a tub of water) should wait until the incision is completely healed (2 to 3 weeks), unless it is possible to sit in the water without getting the incision wet. Soaking in bath water softens the skin at the incision's edges and may allow BACTERIA to gain entrance, causing infection. The full return to normal activities depends on the operation and the person's individual rate of healing and can take place anytime from a few days to 3 months.

See also SURGERY BENEFIT AND RISK ASSESSMENT.

NOSOCOMIAL WOUND INFECTION

About 500,000 of the 27 million Americans who undergo surgery every year develop postoperative wound infections. About 25 percent of postoperative infections are nosocomial (also called iatrogenic)—that is, they occur as a consequence of exposure to pathogens in the hospital environment. Proper wound care minimizes the risk for INFECTION of any kind and supports optimal HEALING.

LIFESTYLE VARIABLES: SMOKING AND OBESITY

The two lifestyle variables that have emerged in recent years as the key causes of preventable disease are smoking and OBESITY. *Each represents a complex mingling of contributory factors, many within the reach of individual control. These variables span health-care specialties; practitioners in nearly all fields of medicine address health issues that derive from either or both. Between them, smoking and obesity account for nearly all preventable* HEART *disease and many types of cancer.*

This section, "Lifestyle Variables: Smoking and Obesity," presents an overview discussion of smoking and obesity as they contribute to health conditions. The entries in this section focus on the health consequences of smoking and obesity, including weight management topics. The section "Nutrition and Diet" features an overview discussion and entries that focus on the broad context of nutrition and diet in health and the development of health conditions. Similarly the section "Fitness: Exercise and Health" features an overview discussion and entries that focus on the broad context of physical activity in health and the development of health conditions.

Lifestyle and Smoking

Cigarette smoking attained social status in the 1920s when soldiers returning from World War I brought their habit home with them. Cigarette smoking became fashionable across social strata, a mark of sophistication and success. But as early as the 1940s doctors recognized that many of their patients who had heart disease or lung disease, including LUNG CANCER, were smokers. Numerous research studies soon confirmed and detailed the specific health risks of smoking, which are extensive. In 1964 the US Surgeon General released the landmark report, *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service,* which presented in fairly stark detail the known and suspected health consequences of cigarette smoking. The report's publication was a wake-up call for doctors as well as the general public, nearly 45 percent of whom were smokers.

Over the next 40 years concerted education efforts resulted in cutting the number of smokers nearly in half. However, the health consequences of smoking skyrocketed. CARDIOVASCULAR DISEASE (CVD) became the leading cause of death, and cigarette smoking was identified as the leading cause of CVD. Lung cancer became the leading cause of death from cancer, and cigarette smoking was identified as the leading cause of lung cancer.

Over the decades, research unequivocally linked cigarette smoking with oral cancer, laryngeal cancer, ESOPHAGEAL CANCER, PANCREATIC CANCER, BLADDER CANCER, PROSTATE CANCER, RENAL CANCER, STOMACH CANCER, and LIVER CANCER. Cigarette smoking proved responsible for most nonallergic ASTHMA, CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), and chronic BRONCHITIS. Researchers also affirmed that ENVIRONMENTAL CIGARETTE SMOKE (secondhand smoke) caused these same health conditions in nonsmokers and was also responsible for most chronic upper respiratory conditions in children.

By the early 2000s many cities in the United States outlawed cigarette smoking in public buildings and restaurants went smoke-free or established separate dining areas for smokers and nonsmokers. Hospitals also banned smoking. By

2004—40 years after the first surgeon general's report on smoking and health—48 million American adults remained smokers, fewer than a quarter of the US adult population, and the number of new smokers reached an all-time low. Nonetheless, cigarette smoking remains the leading cause of CVD, cancer, chronic lung disease, and premature death in the United States.

Lifestyle and Obesity

Cultural and social perceptions strongly influence the extent to which people understand the health risks and consequences of obesity, representing a complex intertwining of personal accountability and societal pressures. Until the 20th century being overweight was a sign of personal prosperity and even a hallmark of health. The corpulent individual was one who could afford unlimited access to food and indulged in its luxury. No correlation as yet existed to link obesity with common and debilitating ailments such as "dropsy" (the generalized edema of congestive HEART FAILURE) and "quinsy" (ANGINA PECTORIS, a symptom of CORONARY ARTERY DISEASE [CAD]). As doctors began to recognize the health implications of obesity a key challenge that emerged was that of convincing people of the connections between health, longevity, and body weight.

Despite what now amounts to decades of scientific evidence, misperceptions persist about the roles of EATING HABITS, food choices, and daily physical activity in WEIGHT LOSS AND WEIGHT MANAGEMENT efforts. Furthermore, food is essential for life—unlike cigarettes and ALCOHOL, which also influence health. One cannot simply stop eating as one can stop smoking or drinking alcohol (which are not easy accomplishments themselves). As is the case with cigarette smoking, the health consequences of obesity accumulate slowly over decades, lulling a person into believing that nothing adverse is happening in his or her body. The first recognition that obesity is a health problem often comes when the doctor diagnoses a health condition such as OBSTRUCTIVE SLEEP APNEA or HYPERTENSION and prescribes weight loss among the treatment recommendations.

For many people with class 2 or 3 obesity, the prospect of losing enough weight to have an effect on health is daunting if not overwhelming and often requires medical assistance. Yet even the loss of 10 or 20 pounds over six months, a goal most people can reach simply by adding 30 minutes of walking to every day's activities, makes a measurable difference in health. Health improvements are apparent almost immediately and extend as weight loss continues. Some people are able to stop taking medications to treat conditions such as hypertension and type 2 DIABETES when their weight reaches healthier levels.

Between 1990 and 1999 the percentage of American adults who have obesity doubled. In 2001 the US Office of the Surgeon General issued *The Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity*, another landmark report identifying obesity as a significant as well as preventable cause of hypertension, type 2 diabetes, ATHEROSCLEROSIS, OSTEOARTHRITIS, and numerous types of cancer. Weight loss became an explicit health objective in HEALTHY PEOPLE 2010, the US national agenda for public health improvement. Many health experts believe obesity, which affects more than 55 million American adults, now rivals cigarette smoking for its deleterious effects on health.

A–B

abdominal adiposity The accumulation of body fat around the middle of the trunk, forming the "apple" body shape or the "spare tire" appearance. Abdominal adiposity has emerged as a pattern of fat storage that correlates to an increased risk for CARDIOVASCULAR DISEASE (CVD) and particularly HEART ATTACK. Doctors assess abdominal adiposity using WAIST CIRCUMFERENCE and WAIST TO HIP RATIO measurements. Reducing abdominal adiposity through weight loss correspondingly lowers related health risks. Abdominal adiposity may become a particular concern for women after MENOPAUSE when hormonal influences can shift fat storage patterns within a woman's body.

A person can be of healthy weight and still have abdominal adiposity because abdominal adiposity is a mechanism of fat distribution in the inner tissues of the abdomen such as around the vital organs. A person who is of healthy weight but who has abdominal adiposity often appears to have a somewhat thickened trunk and thin arms and legs, carrying the traditional "apple" body shape even though he or she does not look overweight. In this circumstance health experts recommend more physical activity to lower the BODY FAT PERCENTAGE. With overall reduction in body fat the trunk stores less fat, lowering the health risks associated with abdominal adiposity.

HEALTH CONDITIONS ASSOCIATED WITH ABDOMINAL ADIPOSITY

ATHEROSCLEROSIS	CORONARY ARTERY DISEASE (CAD)
HEART ATTACK	HYPERLIPIDEMIA
HYPERTENSION	ISCHEMIC HEART DISEASE (IHD)
PERIPHERAL VASCULAR DISEASE (PVD)	type 2 DIABETES

See also ASCITES; BODY MASS INDEX (BMI); BODY SHAPE AND CARDIOVASCULAR DISEASE; DIET AND HEALTH; EXERCISE AND HEALTH; HEALTH RISK FACTORS; LEAN MUSCLE MASS; OBESITY; WEIGHT LOSS AND WEIGHT MANAGEMENT.

bariatric surgery Any of several types of surgical operations to achieve rapid and significant weight loss in people who have morbid OBESITY (obesity severe enough to pose an imminent risk to life). People who weigh 100 pounds or more above healthy weight or who have a BODY MASS INDEX (BMI) of 40 or greater are at severe risk for premature death as well as for health conditions due to obesity. At this level, body fat accounts for one third or more of total body weight. People whose BMIs are between 35 and 40 and who also have CARDIOVASCULAR DISEASE (CVD) or OBSTRUCTIVE SLEEP APNEA are also candidates for bariatric surgery because their obesity is a key contributory factor in these conditions. US surgeons perform about 140,000 bariatric operations a year.

Types of bariatric surgery are either malabsorptive or restrictive, according to the mechanism by which they impede the digestive process. The long-term success rate for maintaining weight loss varies with the kind of OPERATION and the person's commitment to lifestyle changes in EATING HABITS and physical exercise after the surgery. In general the amount of weight loss and the extent of complications are both more significant with malabsorptive operations. Bariatric operations include jejunoileal bypass, biliopancreatic diversion, gastric bypass, and gastric banding.

Surgical Procedure

Open bariatric surgery operations are complex, extensive, and may take several hours for the surgeon to perform. Laparoscopic, or minimally invasive, techniques allow the surgeon to operate

BARIATRIC OPERATIONS

Operation	Benefits	Risks and Complications
jejunoileal bypass (seldom performed)	rapid, significant, and sustainable weight loss reduced health risk for CARDIOVASCULAR DISEASE (CVD), DIABETES, and OSTEOARTHRITIS improvement in existing HYPERTENSION and diabetes	OPEN SURGERY high risk for postoperative complications malabsorption disorders and nutritional deficiencies secondary ANEMIA and OSTEOPOROSIS chronic gastrointestinal discomfort and DIARRHEA LIVER FAILURE kidney stones
biliopancreatic diversion biliopancreatic diversion with duodenal switch	rapid, significant, and sustainable weight loss reduced health risk for CVD, diabetes, and osteoarthritis improvement in existing hypertension and diabetes	open surgery moderate to high risk for operative and postoperative complications intolerance for high protein foods resulting in protein deficiency nutritional deficiencies with risk for anemia and osteoporosis gastric ulcers gastric dumping syndrome belching, abdominal cramping, and FLATULENCE chronic, intermittent diarrhea
Roux-en-Y gastric bypass	rapid, significant, and sustainable weight loss reduced health risk for CVD, diabetes, and osteoarthritis improvement in existing hypertension and diabetes	open surgery moderate risk for operative and postoperative complications nutritional deficiencies VOMITING gastric dumping syndrome PEPTIC ULCER DISEASE
vertical banded gastroplasty	laparoscopic surgery reversible rapid and significant weight loss for people who also make appropriate lifestyle changes	slight risk for operative and postoperative complications staple failure occasional gastric dumping syndrome gastric pouch can expand with continued excessive food consumption
adjustable gastric banding	laparoscopic surgery adjustable and reversible rapid recovery and return to normal activities gastrointestinal structure remains unchanged	balloon failure infection at the banding site slower and less consistent weight loss than with other bariatric operations gastric pouch easily expands with excessive food consumption up to 20 percent of people may experience no weight loss

through several small incisions called ports and generally require less time in the operating room. The stay in the hospital after bariatric surgery varies from a day for laparoscopic banding operations to five days or longer for open gastric bypass or biliopancreatic diversion operations. Full recovery and return to normal activities can take several months, though many people are able to return to most routine activities and to work in four to six weeks.

Jejunoileal bypass Jejunoileal bypass is a malabsorption operation. The first weight-reduction operation surgeons performed, the jejunoileal bypass joins the first part of the SMALL INTESTINE's second segment, the JEJUNUM, to the last part of the small intestine's third segment, the ILEUM. This bypasses the stretch of small intestine where most nutrient absorption takes place, rerouting food relatively undigested on a direct path from the STOMACH to the end of the small intestine and into the COLON. Though successful in generating significant weight loss jejunoileal bypass has numerous unpleasant side effects, including chronic and sometimes persistent or severe DIARRHEA, MALNUTRITION, electrolyte imbalance, and small bowel obstruction (ILEUS). Because of the high rate of complications with jejunoileal bypass and the current availability of other weight loss operations, surgeons in the United States seldom perform jejunoileal bypass today.

Biliopancreatic diversion Biliopancreatic diversion combines restriction and malabsorption. Developed as an improvement over jejunoileal bypass, the operation involves removing a portion of the stomach to reduce the volume of food it can hold as well as bypasses the central segment of the small intestine to curtail absorption during digestion. The surgery may be open or laparoscopic (minimally invasive). The first segment of the small intestine, the DUODENUM, connects the stomach to the small intestine and also serves as the conduit through which the PANCREAS channels DIGESTIVE ENZYMES and the GALLBLADDER empties BILE.

In straight biliopancreatic diversion, the surgeon removes the lower two thirds of the stomach and connects the remaining third directly to the ileum, the end portion of the small intestine near its junction with the colon. The stomach becomes a very small pouch, restricting the amount of food that can enter the gastrointestinal tract. The digestive process bypasses most of the small intestine, limiting absorption.

A variation of this operation is biliopancreatic diversion with duodenal switch. In this operation the surgeon divides the stomach about in half lengthwise, creating a pouch between the ESOPHAGUS and the duodenum. The surgeon then divides the duodenum in half lengthwise and reconstructs it into two narrow, tubelike structures. One of these structures drains digestive enzymes from the pancreas and bile from the gallbladder into the gastrointestinal tract. The surgeon joins the other to the end portion of the ileum near the colon. Biliopancreatic diversion with duodenal switch allows better absorption in the remaining segment of small intestine of NUTRIENTS such as protein, vitamins, calcium, iron, and fat.

Gastric bypass Gastric bypass operations severely restrict food consumption by reducing the size of the stomach to a small pouch that can hold about 0.5 ounce (15 milliliters); the stomach normally holds about 50 ounces (1.5 liters). The most common and successful gastric bypass operation is the Roux-en-Y gastric bypass, a complex operation in which the surgeon divides the stomach to form two segments and reroutes the small intestine. Both segments of the stomach remain functional. The upper segment is a small gastric pouch with a capacity of 0.5 to 1 ounce. The surgeon joins the jejunum to the bottom of the pouch, bypassing the primary absorptive segment of the small intestine. The lower segment of the stomach retains the duodenum, which the surgeon restructures to join the jejunum near the ileum. The duodenum feeds digestive enzymes and DIGESTIVE HORMONES into the jejunum to aid in the absorption of nutrients.

Gastric banding Like gastric bypass operations, gastric banding operations reduce the stomach to a small pouch that can hold about 0.5 ounce and narrow the outlet at the base of the stomach to slow the passage of food from the stomach to the small intestine. Gastric banding significantly limits the volume of food the person can consume; exceeding the limit causes VOMITING. Surgeons

most commonly perform two types of gastric banding operations.

- Vertical gastric banding (VGB), also called vertical banded gastroplasty, partitions the stomach into two vertical segments. Surgical staples separate the segments, leaving a narrow channel between them. The small gastric pouch limits the amount of food the person can consume. A silicone band constricts the channel between the two gastric chambers to significantly slow the flow of food from the upper gastric pouch to the lower segment of the stomach. Food travels through the gastrointestinal tract in the normal way though moves through the stomach much more slowly than normal.
- Adjustable gastric banding (AGB), also called lap banding, partitions the stomach solely through the use of an inflatable silicon band applied so that it creates a gastric pouch that can hold about 1 ounce. A narrow catheter extends from the band to a port implanted beneath the SKIN. The surgeon gradually inflates the balloon with sterile saline during follow-up office visits to increase constriction of the stomach.

Gastric banding operations are laparoscopic, greatly reducing operative and postoperative risks and complications, and have the added benefit of being reversible. Most people return to normal activities within four weeks after the surgery. However, gastric banding has the lowest success rate among the bariatric operations. Weight loss is more gradual than with other operations. Over time the stomach can stretch to hold considerably more volume, depending on how much food the person attempts to consume on a consistent basis. Because food continues to the small intestine and digestion of it remains unaffected, a person who consumes high-CALORIE foods after a gastric banding operation may end up losing little if any weight.

About 80 percent of people who undergo gastric banding operations lose weight after surgery and about 50 percent reach the goal of losing 50 percent of their excessive weight within the first year after surgery. About 20 percent, however, do not lose weight because their lifestyle habits remain unchanged and their stomachs quickly regain capacity.

Risks and Complications

Any bariatric operation is major surgery with inherent risks, including excessive bleeding during or after the operation and INFECTION. Infection in the early postoperative period is a particular risk with any surgery on the gastrointestinal tract. Leakage of gastrointestinal contents into the abdominal cavity can cause PERITONITIS, a potentially life-threatening infection of the membrane that lines the abdominal cavity. Emergency surgery may be necessary to treat peritonitis. BLOOD clots may break free from blood vessels at the operative site, traveling through the body until they lodge in blood vessels too narrow to carry them any farther. Blood clots can occlude (block) arteries or veins anywhere in the body, including the LUNGS (PULMONARY EMBOLISM), BRAIN (STROKE), and HEART (MYOCARDIAL INFARCTION).

Though the risk dying as a consequence of bariatric surgery is less than 1 percent, many people who have OBESITY also have other health conditions that increase their risk profile. It is important to fully understand the risks of surgery compared to the risks of the obesity.

About 50 percent of people who undergo bariatric surgery experience complications after the operation, most of which are manageable postoperatively though may become chronic. Malabsorptive operations that bypass the small intestine have high risk for vitamin, mineral, and protein deficiencies. One in three people who undergo a weight loss operation develops chronic nutritional deficiencies with long-term health consequences such as OSTEOPOROSIS and ANEMIA. One in five requires additional surgery to repair problems such as fistula (abnormal opening) or HERNIA. The rapid weight loss of bariatric surgery triggers GALLBLADDER DISEASE, especially the formation of gallstones, in half of people who undergo bariatric surgery.

Milder common complications include GASTROESOPHAGEAL REFLUX DISORDER (GERD); belching;

chronic gastrointestinal discomfort; and gastric dumping syndrome, a reaction of the gastrointestinal tract to eating high concentrations of sugar (sweets) and protein (meats). Excessive body weight stretches the skin, which may sag and fold after extensive weight loss. About 30 percent of people who undergo bariatric surgery subsequently have PLASTIC SURGERY operations such as panniculectomy and abdominoplasty to remove excess skin after weight loss.

Outlook and Lifestyle Modifications

Most people require four to eight weeks for full recovery from bariatric surgery and return to regular activities. Some people may require longer, particularly those who experience postoperative complications. The changes to the gastrointestinal system that bariatric surgery makes are permanent and alter the way the digestive process functions, sometimes in ways that require ongoing medical care and medications. Many people will also need to continue taking medications to treat conditions they had before surgery, such as HYPERTENSION and DIABETES.

For several weeks to several months, people who have gastric bypass procedures to restrict the size of the stomach must eat liquid or pureed foods to give their gastrointestinal tracts time to adjust. The gastric pouch can hold such a limited volume that it often is necessary to separate eating and drinking by 30 to 60 minutes. As well, the person must thoroughly chew food before swallowing, as the gastric pouch lacks the MUSCLE capacity and size to participate in further breaking down the size of food particles.

Despite the changes to the gastrointestinal system's structure and function, lifestyle factors such as food choices and physical exercise remain important for long-term weight management. The success of bariatric surgery for maintaining weight loss depends on the extent to which an individual makes the necessary changes in these factors. Doctors consider bariatric surgery successful when the person maintains weight loss of 50 percent of excess body weight for five years after surgery. Though many people may lose 100 pounds or more with bariatric surgery, they may remain overweight though at a healthier weight than before surgery.

In general, people who undergo bariatric operations lose 50 percent of excess body weight in the first year after surgery. The rate of weight loss depends on the type of operation and tends to be most dramatic with gastric bypass operations. Weight loss tends to peak around three years after surgery, at 70 to 85 percent of excess body weight. Five years after surgery, however, about 70 percent of people have regained weight to about 50 percent of the excess (which still falls within the parameters for successful surgery) and about 5 percent of people have regained all of their lost weight. Doctors attribute these results largely to continuation of poor eating habits and physical inactivity. Food choices and daily exercise are essential to sustain weight loss over the long term.

Outcome studies of bariatric operations show evidence that people who maintain their weight loss lower their risk for CVD and type 2 diabetes to the same extent as people who lose the weight through nonsurgical methods. Because weight loss is so dramatic, some people are able to manage mild to moderate hypertension and type 2 diabetes through lifestyle alone, ending the need for medications. Researchers believe such findings further support the role of obesity as an independent risk factor for these conditions as well as demonstrate the health value of WEIGHT LOSS AND WEIGHT MANAGEMENT.

See also DIET AIDS; DIET AND HEALTH; DIETING; EATING DISORDERS; LIFESTYLE AND HEALTH; MALABSORPTION; MINERALS AND HEALTH; MINIMALLY INVASIVE SURGERY; NUTRITIONAL NEEDS; OBESITY AND HEALTH; SURGERY BENEFIT AND RISK ASSESSMENT; VITAMINS AND HEALTH.

body fat percentage The proportion of the body's composition that is fat. Body fat percentage is an indirect indicator of LEAN MUSCLE MASS and correlates to health circumstances such as FERTILITY as well as health conditions such as type 2 DIABETES and CARDIOVASCULAR DISEASE (CVD). The body requires a minimum amount of fat for its functions and activities, generally about 4 percent for men and 12 percent for women. Body fat percentage above 25 percent for men and 32 percent for women correlates with OBESITY. A high body fat percentage in combination with ABDOMINAL ADIPOSITY (the "apple" body shape) portends a particularly high risk for CVD, HEART ATTACK, and STROKE.

BODY FAT PERCENTAGE AND HEALTH RISK

Health Status	Men	Women
at risk for NUTRITIONAL DEFICIENCY	< 4 percent	< 12 percent
lean (athlete or high fitness level), no increased health risk	4 to 15 percent	12 to 22 percent
healthy, no increased health risk	< 20 percent	< 27 percent
overweight, moderate increase in health risk	20 to 25 percent	27 to 32 percent
OBESITY, significant increase in health risk	> 25 percent	> 32 percent

Methods for measuring or approximating body fat percentage include

- BODY MASS INDEX (BMI), a mathematical formula based on weight and height
- skinfold calipers, which measure the thickness of a fold of SKIN (typically at the triceps on the back of the upper arm) to determine the amount of subcutaneous fat
- bioelectrical impedance, which measures the resistance a mild electrical current encounters when passed through the body
- hydrostatic weighing, which uses water displacement to determine body mass

Additional measures that improve the precision of body fat percentage estimates include WAIST CIRCUMFERENCE and WAIST TO HIP RATIO, as these measures increase with excessive body fat. Dual-energy X-RAY absorptiometry (DEXA), an X-ray procedure to determine BONE DENSITY as an assessment of OSTEOPOROSIS, also provides calculations of body fat percentage and lean tissue mass. No single method provides an absolute measure of body fat percentage.

See also DIET AND HEALTH; EXERCISE AND HEALTH; FITNESS LEVEL; UPPER ARM CIRCUMFERENCE; WEIGHT LOSS AND WEIGHT MANAGEMENT.

body mass index (BMI) A mathematical measure of total body size and its correlation to health risk. BMI values derive from height (without shoes) and weight (without clothes) measures, with mathematical calculations that convert those measures to a value that reflects overall body size. BMI represents the mass of the body in kilograms per meter squared (kg/m^2) though the common presentation of BMI is simply the numeric value. A low or a high BMI corresponds with increased risk for numerous health conditions. A BMI of 25 or greater is overweight; a BMI of 30 or greater is OBESITY. BMI values apply to men or women who have the same measurements. For example, a

BMI AND HEALTH RISK

BMI	Classification	Health Risk Due to Weight
> 18.5	underweight	may indicate EATING DISORDERS or undernutrition
19 to 24.9	healthy weight	no increased health risk
25 to 29.9	overweight	moderate health risk
30 to 34.9	OBESITY, class 1	significant health risk
35 to 39.9	obesity, class 2	high health risk; INSULIN RESISTANCE or CARDIOVASCULAR DISEASE (CVD) likely
40+	obesity, class 3	severe health risk; DIABETES, CVD, or HYPERTENSION likely

man who is 5 feet 8 inches tall and weighs 175 pounds has the same BMI as a woman who is 5 feet 8 inches tall and weighs 175 pounds.

For most people a high BMI indicates increased body fat. The higher the BMI is above the "healthy" range, the greater the health risk for HYPERTENSION (high BLOOD PRESSURE), type 2 DIABETES, and forms of CARDIOVASCULAR DISEASE (CVD) such as HYPERLIPIDEMIA, ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD). Risk for these conditions further increases when WAIST CIRCUMFERENCE also is greater than 40 inches for men and 35 inches for women, though waist circumference is itself an independent risk factor for the same health conditions. Losing weight drops BMI and reduces health risk.

BMI values may not be accurate in children, the elderly, and performance athletes because body mass may not correctly reflect body composition. The elderly may have more body fat than BMI indicates, with a correspondingly higher health risk. Performance athletes (amateur or professional) typically have higher LEAN MUSCLE MASS (large skeletal muscles) and lower body fat percentages than less physically active people of the same weight; the increased MUSCLE mass raises the BMI even though body fat is lower.

See also ABDOMINAL ADIPOSITY; CHILDHOOD OBESITY; DIET AND HEALTH; EXERCISE AND HEALTH; LIFESTYLE AND HEALTH; NUTRITIONAL ASSESSMENT; NUTRITIONAL NEEDS; OBESITY AND HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

BODY MASS INDEX (BMI)

BMI	**19**	**20**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**	**41**	**42**	**43**	**44**	**45**
Height (inches)	Body Weight (pounds)																										
58	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167	172	177	181	186	191	196	201	205	210	215
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173	178	183	188	193	198	203	208	212	217	222
60	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179	184	189	194	199	204	209	215	220	225	230
61	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185	190	195	201	206	211	217	222	227	232	238
62	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191	196	202	207	213	218	224	229	235	240	246
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197	203	208	214	220	225	231	237	242	248	254
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204	209	215	221	227	232	238	244	250	256	262
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210	216	222	228	234	240	246	252	258	264	270
66	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216	223	229	235	241	247	253	260	266	272	278
67	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223	230	236	242	249	255	261	268	274	280	287
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	216	223	230	236	243	249	256	262	269	276	282	289	295
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236	243	250	257	263	270	277	284	291	297	304
70	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243	250	257	264	271	278	285	292	299	306	313
71	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250	257	265	272	279	286	293	301	308	315	322
72	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258	265	272	279	287	294	302	309	316	324	331
73	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265	272	280	288	295	302	310	318	325	333	340
74	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272	280	287	295	303	311	319	326	334	342	350
75	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279	287	295	303	311	319	327	335	343	351	359
76	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287	295	304	312	320	328	336	344	353	361	369

Adapted from U.S. National Heart, Lung, and Blood Institute (NHLBI) Obesity Education Initiative (2005)

childhood obesity The development of unhealthy body weight due to excessive body fat before adulthood (age 18). Childhood OBESITY has numerous health consequences that affect METABOLISM, physical growth and development, and PUBERTY. Childhood obesity jumped significantly between 1970 and 2000. Currently 15 percent of US children have obesity. Another 20 percent are overweight, which places them at risk for obesity.

Health experts attribute the rise in childhood obesity primarily to EATING HABITS and physical inactivity. Ongoing health assessment monitoring, such as the periodic National Health and Nutrition Examination Survey (NHANES) and the Behavioral Risk Factor Surveillance System (BRFSS), reveals a steady decline in the level of physical activity among young people, including through physical education programs in the schools. Increasing the physical activity of children as a mechanism for improving long-term health is among the objectives of HEALTHY PEOPLE 2010, the US government's agenda for community health. Researchers also continue to explore other factors that may contribute to obesity. Much attention focuses on the role of genetics and regulation of metabolic processes within the body such as the release and activity of hormones.

Diagnosing Childhood Obesity

Conventional methods of assessing BODY FAT PERCENTAGE and BODY MASS INDEX (BMI), the standard measures of obesity, are somewhat different for children from those used for adults. A child's body fat varies with developmental stages and growth cycles. Correspondingly, a child's BMI varies according to age and developmental stage. As well, boys and girls have different body fat composition through the end of ADOLESCENCE.

In 2001 the US Centers for Disease Control and Prevention (CDC) developed gender-specific BMI-for-age charts to provide guidelines for assessing underweight, healthy weight, and overweight in children between the ages of 2 and 20. The charts correlate BMI to percentile, a measure of relative comparison that allows monitoring of BMI through the entire course of childhood. The boundary for overweight is the 85th percentile (85 percent of children who are the same age and gender have a lower BMI) and for obesity the 95th percentile (95 percent of children who are the same age and gender have a lower BMI).

Health Implications of Obesity in Childhood

Doctors are seeing INSULIN RESISTANCE, type 2 DIABETES, HYPERTENSION (high BLOOD PRESSURE), HYPER-

BMI FOR AGE FOR CHILDREN AND TEENS: KEY PERCENTILE MARKERS

BMI for Age: Boys/Girls				BMI for Age Percentile	Health Status for Body Weight
2 years	7 years	15 years	20 years		
14.8/14.4	13.7/13.4	16.6/16.3	19.1/17.8	5th	underweight
18.2/18.0	17.4/19.2	23.4/24.0	27.1/26.5	85th	overweight or at risk for overweight
19.3/19.1	19.1/19.6	26.8/28.1	30.6/31.8	95th	obesity

LIPIDEMIA, OSTEOARTHRITIS, and the beginnings of ATHEROSCLEROSIS in an increasing number of children, especially adolescents, who have obesity. These conditions may require treatment with medications and other interventions, the long-term health consequences of which remain unknown. Emotional, social, and self-esteem issues also are common among children who have obesity. The stigma of being "fat" is a difficult challenge for children who are forming their sense of self and are especially sensitive to peer acceptance and rejection. Obesity may result in a young person feeling ostracized in school and having difficulty forming friendships.

Health Implications of Childhood Obesity in Adulthood

Increasing evidence points to long-term health consequences for people who enter adulthood with obesity. Childhood obesity correlates with increased risk for earlier onset in adulthood of insulin resistance and type 2 diabetes, osteoarthritis, hypertension, hyperlipidemia, atherosclerosis, CORONARY ARTERY DISEASE (CAD), STROKE, and certain cancers. An increased risk for these conditions may exist even among people who had childhood obesity yet achieve relatively healthy weight as adults. These health conditions account for significant physical disability and further complications resulting from co-morbidities (the cascading consequences of co-existing, multiple health conditions).

Treatment Approaches and Outlook

Prevention of obesity is the first line of treatment. Routine childhood health examinations monitor a child's growth and development. Intervention for children who have BMI-for-age values near or at the 85th percentile can head off obesity. Lifestyle modifications—nutritious eating habits and increased physical exercise—presented in a positive context represent the most effective approach for long-term weight management. However, obesity is a complex condition that requires individualized assessment and a treatment approach that accommodates the various factors relevant for a child. Counseling and SUPPORT GROUPS may help address DEPRESSION, emotional issues, and family dynamics.

Positive reinforcement must frame treatment approaches for OBESITY in children. Punitive approaches such as withholding food, criticizing the child, and forcing exercise are inappropriate and can have serious emotional and psychologic consequences for the child.

Established obesity is a more difficult challenge for treatment, though lifestyle modifications remain the mainstay of therapeutic approaches. Nutrition education and BEHAVIOR MODIFICATION THERAPY are helpful for older children, especially adolescents. Many health experts recommend involving the entire family in the effort to shift to healthful lifestyle habits. Older adolescents who struggle with obesity may benefit from medications intended to suppress APPETITE. Many eating disorder treatment programs offer comprehensive treatment that targets the child's individual circumstances and needs. BARIATRIC SURGERY, a treatment option for adults who are otherwise unable to treat their obesity, is not usually an option for young people.

There is every reason to believe the health outlook for children who achieve healthy weight and enter adulthood at healthy weight is excellent. Health experts are hopeful that lifestyle modifications implemented early in life will carry through adulthood, helping reduce adult obesity as well.

See also DIET AND HEALTH; EXERCISE AND HEALTH; OBESITY AND HEALTH; QUALITY OF LIFE; WEIGHT LOSS AND WEIGHT MANAGEMENT.

D–E

diet aids Products that claim to expedite weight loss. Diet aids may be products proclaimed as APPETITE suppressants (decrease the urge to eat) or products or electronic devices advertised to "burn away" fat. Though most such diet aids have limited or no value, the diet aid industry in the United States generates about $30 billion in annual sales.

Over-the-counter appetite suppressants typically contain diuretics (drugs that increase URINATION), STIMULANTS such as pseudoephedrine (a decongestant) and CAFFEINE, or bulking agents that draw water after consumption and purport to instill a sense of fullness. These kinds of products may have a limited effect to decrease appetite though may have undesired side effects such as agitation and mucous membrane dryness.

Devices that claim to burn energy by stimulating MUSCLE fibers to contract may indeed stimulate muscle contraction but do not generate enough energy to affect the body's metabolic balance. Wraps, creams, and other substances applied to the SKIN that proclaim to "melt away" fat lack scientific basis for their claims. Many diet aids come with diet plans that advise increased exercise and reduced food intake—the only proven method for weight loss.

See also DIET AND HEALTH; DIETING; "FAT BURNERS"; NUTRITIONAL NEEDS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

dieting The practice of temporarily altering one's food intake to achieve weight loss. Dieting approaches typically restrict calories and often food types. Though such approaches are effective for short-term weight loss, they are not sustainable in the long term and many people regain the lost weight in less time than it took to lose it. Weight loss as a component of long-term weight management requires lifestyle modifications that dieting does not accommodate, such as increased physical exercise and EATING HABITS that foster healthful food choices.

Dieting tends to focus on restricting foods that are high in calories, such as carbohydrates and fat. Depriving the body of CALORIE intake forces it to draw from stored energy sources such as glycogen and body fat, though severe calorie restriction (less than 800 calories a day) results in protein METABOLISM and loss of LEAN MUSCLE MASS because protein is easier for the body to convert to GLUCOSE to meet its energy needs. Restrictive dieting is likely to deprive the body of other needed NUTRIENTS such as vitamins and minerals, and commonly results in food cravings for items the diet does not allow.

Some dieting approaches are detrimental to health over time. High-fat, low-carbohydrate diets may achieve short-term weight loss but are likely to result in increased levels of cholesterol and triglycerides in the BLOOD circulation, raising the risk for HYPERLIPIDEMIA and ATHEROSCLEROSIS regardless of weight loss. As well, low-carbohydrate diets cause the body to excrete more water than usual, resulting in weight loss but not loss of body fat. "Yo-yo" dieting, in which weight continually fluctuates, is particularly harmful not only for long-term weight management but also for the glucose–INSULIN balance, generating increased risk for INSULIN RESISTANCE. There is also the tendency to regain the lost weight as well as additional weight as somewhat of a rebound response in the form of excessive eating when the restrictive diet ends.

People who have class 2 or 3 OBESITY, in which adverse health conditions are either imminent or already exist because of excessive body weight,

may benefit from a doctor-supervised, short-term restrictive diet as part of an overall weight management approach. However, the most effective form of dieting for sustained weight loss and improved health status is that which combines moderately reduced caloric intake and increased daily exercise. Though weight loss is gradual with such an approach (health experts recommend one half to one pound a week), it is more likely to be permanent because it arises from lifestyle modifications that are themselves sustainable.

See also APPETITE; DIET AND HEALTH; EATING DISORDERS; EXERCISE AND HEALTH; HUNGER; NUTRITIONAL NEEDS; OBESITY AND HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

eating habits The ways in which an individual approaches food consumption. Eating habits encompass factors such as food choices, the timing and frequency of meals and snacks, portion size, and social practices around eating (such as sitting down as a family to eat meals at the table or eating while watching television). Eating habits affect nutrition, body weight, and body composition.

Why People Eat

Much eating occurs for reasons other than to bring energy and NUTRIENTS into the body. People may eat

- for emotional comfort
- for something to do or social interaction, such as going out to eat
- out of habit, such as because it is meal time
- because other people are eating
- because a particular item of food smells or looks good
- to satisfy a food craving

These eating habits are not always easy to break. Recognizing them is the first step; changing them often requires understanding the reasons behind them. Increasing physical activity helps accommodate extra calories consumed and also provides diversion to direct interest elsewhere.

How—and How Much—People Eat

Portion size is a key factor in healthy eating. Many people overestimate the amount of food that constitutes a serving and underestimate how much food they eat. Product labels specify the number size of servings the package contains. However, much packaging gives the appearance of a single serving when the label specifies several servings. It is important to carefully read labels and to purchase packaged products that truly contain a single serving, that several people can share, or that are easy to store.

Portion sizes are especially difficult to assess for home-cooked meals. For example, a single serving of meat is 3 ounces, about the size of a deck of cards. Yet most people eat a portion that is 8 to 12 ounces or more, which is equivalent to 2½ to 4 servings. A single serving portion of cooked rice or mashed potatoes is 1/2 cup, though the typical serving spoon dishes up more than that. A person who pours a bowlful of cereal with milk for breakfast is likely eating 2 to 4 servings of each. Even a few handfuls of chips eaten from the bag likely constitute 3 or 4 servings. As well, many people feel compelled to eat all the food on their plates.

What People Eat

Nutritional guidelines recommend the highest proportion of foods come from fruits, vegetables, whole grains and whole grain products, and low-fat proteins. However, fats and carbohydrates make up the majority of dietary intake for many people. In the United States the frequency with which people eat in restaurants, sit down as well as fast food, is very high. Though a number of restaurants offer fresh vegetables and fruit and feature "heart healthy" menu choices, restaurant meals tend to be high in both fat and carbohydrate. The same is true of snack foods and prepared foods such as frozen dinners and boxed and canned products.

When People Eat

Eating when hungry is the ideal timing for the body but is often fraught with challenge in real life. Because APPETITE is as much a factor of desire to eat as a signal of the body's need to acquire nutrients, most people have difficulty distinguishing genuine hunger. The urge to eat, particularly when delayed, tends to manifest as overconsumption. Some people try to eat only one meal as a

means of controlling how much they eat, though this is a counterproductive effort because when they eat they are so hungry that they eat too much and often less than nutritious foods. Other people may eat full meals at breakfast, lunch, and supper because it is the pattern of eating they have always followed. Snacking between meals and eating on the go are habits that often result in overeating as well as high-fat, high-carbohydrate consumption.

Establishing and Maintaining Health-Oriented Eating Habits

Planning for meals often instills a sense of calm around the process of eating because the planning helps take away the pressure of figuring out what to eat and how to make the meal happen. Household members can take turns being responsible for meals, sharing both the responsibility and the pleasure of the meal. Most people do better nutritionally when they eat five smaller meals spread throughout the day, though personal schedules may make such an approach impractical, or three meals a day with nutritious snacks between.

See also DIET AND HEALTH; FOOD CRAVINGS; NUTRITIONAL NEEDS; WEIGHT LOSS AND WEIGHT MANAGEMENT.

"fat burners" Products—foods, drinks, supplements, devices, and other items—that proclaim to reduce body fat without exercise or changes in diet. Such products are not effective in this manner; the only method for "burning" fat is for a person to expend more energy through activity than he or she consumes through eating. Some "fat-burner" products contain diuretics (substances that draw fluid from the body to increase URINE output). Some "fat burners" claim to spot-reduce, or eliminate fat in a targeted fashion. For the most part such claims are at best inaccurate and more often deceptive. The body does not draw fat from one location any more than another during weight loss efforts. Rather the body draws fat from fat stores throughout the body. Fat accumulates in larger amounts in certain parts of the body because these areas have more fat cells to accept lipid storage. These areas tend to be the abdomen, hips, buttocks, thighs, and upper arms. When weight loss occurs, correspondingly more fat leaves these areas. As well, fat loss in these areas is more apparent because the fat collects in layers just underneath the SKIN. Fat loss from the cheeks and neck also appears noticeable early in the weight loss process.

See also DIET AIDS; DIETING; WEIGHT LOSS AND WEIGHT MANAGEMENT.

food cravings The desire to eat particular foods, typically without correlation to HUNGER or APPETITE. Some people speculate that food cravings suggest certain substances are missing from the diet or from consumption, such as salt when a person craves salty foods. Others believe food cravings originate as signals the BRAIN sends to satisfy its pleasure centers. Changes in HORMONE levels in the body, such as occur during PREGNANCY, appear to initiate cravings for foods in sometimes unusual combinations. Food aversions are also common in pregnancy. Pica is the condition of craving nonfood substances such as dirt or paper and may indicate an iron deficiency.

Other food cravings appear emotionally driven, such as those for comfort foods during times of emotional distress. For the most part, however, there are no clear scientific explanations for food cravings, and everyone experiences them at some time. As long as a person continues to eat an overall nutritious diet, succumbing occasional food cravings has no detrimental effect on health. However, uncontrolled response to food cravings may result in nutritional imbalances and often is a key factor in overeating, overweight, and OBESITY. It may also signal underlying emotional or psychological disturbances.

Controlling food cravings is challenging and highly personalized. Methods that are effective for some people include

- diversionary activities that make succumbing to the craving difficult (such as taking a walk or bicycle ride)
- eating healthful alternatives to the desired food (such as fresh fruit instead of candy or lemon instead of salt for seasoning)
- HYPNOSIS to fortify the resolve to resist the craving

- eating regular meals throughout the day that contain a balance of nutritious foods
- eating a small serving or portion of the desired food, such as a mini-size instead of a full-size candy bar
- BEHAVIOR MODIFICATION THERAPY to gain insight and understanding about the reasons for craving foods

See also ANEMIA; EATING DISORDERS; EATING HABITS; MORNING SICKNESS; SATIETY.

lean muscle mass The amount of body tissue that is lean MUSCLE in contrast to the percentage that is body fat. There is an inverse relationship between lean muscle mass and BODY FAT PERCENTAGE, such that when one increases the other decreases. Lean muscle mass increases with regular physical exercise that challenges muscle fibers to expand. Serious illness or injury, such as significant BURNS or major trauma, may draw protein from lean muscle mass to aid in HEALING, resulting in diminished lean muscle mass. A common method for estimating lean muscle mass is UPPER ARM CIRCUMFERENCE, a measurement of the distance around the middle of the upper arm. It is also possible, though less accurate, to approximate lean muscle mass based on body fat percentage determinations. The X-RAY procedure dual-energy X-ray absorptiometry (DEXA), a diagnostic test that measures BONE DENSITY, also provides data for calculating lean muscle mass.

See also BODY MASS INDEX (BMI); RESISTANCE EXERCISE; WAIST CIRCUMFERENCE; WAIST TO HIP RATIO.

nicotine replacement Products intended to wean a person from NICOTINE otherwise acquired through cigarette smoking. Nicotine is a highly addictive DRUG that occurs naturally in tobacco. Though behavior is an important component of smoking, the addictive quality of nicotine accounts for the difficulty people have in quitting. Nicotine replacement can be fairly effective as an aid for SMOKING CESSATION. The premise is that the nicotine in the product, though less than that in a cigarette, fulfills the body's desire for nicotine when the person stops smoking.

Most nicotine replacement products come in diminishing strength doses so over the course of a typical smoking cessation program (usually 12 weeks) the person takes decreasing doses to ease the body's dependence on the nicotine. Nicotine replacement products include

- transdermal (SKIN) patches, which a person wears for 16 to 24 hours to deliver a steady trickle of nicotine absorbed through the skin
- chewing gums, which deliver doses of nicotine with timed chewing and holding the gum between the gum and cheek for absorption of the released nicotine through the tissues of the MOUTH and into the BLOOD circulation
- lozenges, which release nicotine as they dissolve in the mouth for absorption through the tissues of the mouth and into the blood circulation
- nasal sprays, which deliver nicotine to the membranes inside the NOSE for rapid absorption into the blood circulation
- inhalers, small plastic mouthpieces that hold cartridges containing nicotine a person draws in through the mouth similar to smoking a cigarette; nicotine enters the blood circulation by absorption through the tissues of the mouth (not the LUNGS)

Taking NICOTINE replacement products in combination with one another or while still smoking cigarettes presents a major risk for nicotine toxicity. Symptoms of nicotine overdose include

- **PALPITATIONS**
- **rapid or irregular HEART RATE**
- **NAUSEA**
- **DIARRHEA**

Nasal sprays and inhalers require a doctor's prescription. Transdermal patches and chewing

gums are available over the counter as well as by prescription, depending on the strength (nicotine DOSE). With all nicotine replacement products nicotine OVERDOSE can occur if the person combines nicotine products or continues to smoke or use other tobacco products (such as chewing tobacco or cigars) while using a nicotine replacement product. It is important to keep nicotine replacement products, especially gums and lozenges, out of the reach of children.

Other possible side effects include local irritation of the tissues, HICCUPS with the gum or lozenges, and COUGH with any nicotine replacement product except transdermal patches. Some people may develop dependence on the nicotine replacement product, which is more of a risk with nasal sprays and inhalers because these methods deliver nicotine rapidly to the blood circulation in similar fashion as cigarette smoking. The typical course of smoking cessation therapy with nicotine replacement is 12 to 16 weeks and should not extend longer than 6 months.

See also ADDICTION; ANTISMOKING EFFORTS; SMOKING AND HEALTH.

obesity The circumstance of weighing 20 percent or greater in excess of ideal or healthy weight as a consequence of excessive body fat. Doctors consider a BODY MASS INDEX (BMI) of 30 to be the boundary of obesity. In the 1990s health experts classified obesity as a clinical diagnosis as well as an independent risk factor for numerous health conditions, including DIABETES, GALLBLADDER DISEASE, HYPERTENSION (high BLOOD PRESSURE), ATHEROSCLEROSIS, HEART FAILURE, HORMONE-DRIVEN CANCERS of the BREAST and PROSTATE GLAND, and CORONARY ARTERY DISEASE (CAD). Obesity also interferes with INSULIN sensitivity and with HEALING. Many researchers believe obesity is as significant a risk factor as cigarette smoking for CARDIOVASCULAR DISEASE (CVD).

Causes of Obesity

The simple cause of obesity is more intake than outgo—energy from food consumed exceeds energy expended through physical activity. However, the circumstances that establish this imbalance are complex. Lifestyle factors—EATING HABITS and physical inactivity—are key causes of obesity. The extent to which genetic factors influence obesity remains unknown, though researchers have identified gene-directed processes that regulate many of the variables within the body responsible for how the body uses and stores energy. Social, cultural, emotional, and psychologic issues further influence the development of obesity.

Genetic factors Researchers have discovered a number of genes that regulate body functions related to APPETITE and METABOLISM. One is the *ob* GENE, which regulates the production of the HORMONE leptin. Leptin suppresses the HUNGER, appetite, and SATIETY centers in the HYPOTHALAMUS and brainstem. Certain mutations of the *ob* gene result in diminished sensitivity of the leptin receptors to leptin, reducing leptin's effectiveness. Other mutations influence the production of leptin. Leptin also influences the actions of another protein, neuropeptide Y (NPY), that stimulates appetite. Researchers believe mutations of the *ob* gene predispose individuals to obesity because appetite control mechanisms within the body do not function properly. However, these mutations do not unequivocally cause obesity.

Social and cultural influences Many people who meet the diagnostic criteria for obesity do not recognize that their weight has become a health condition with serious consequences if untreated. About two thirds of people who have obesity identify themselves as such; one third perceive themselves as overweight but not to an extent that interferes with health or exceeds their ability to manage by losing weight at will. There is a social tendency to joke about excessive weight, diminishing its significance as a health factor with a corresponding cultural shift toward accommodating larger body size.

Emotional and psychologic factors The reasons people eat often have little to do with hunger or nutritional need. Eating can provide a sense of comfort during times of emotional stress. Overeating is an eating disorder that often has complex psychologic foundations related to issues of self-esteem, control, or psychologic injury such as may occur as a consequence of sexual, domestic, or childhood abuse.

Symptoms and Diagnostic Path

The primary symptom of obesity is significantly increased body size due to excessive body fat. The diagnostic markers for obesity include

- BMI of 30 or greater

- body fat percentage greater than 25 percent for men or 32 percent for women
- WAIST CIRCUMFERENCE greater than 40 inches for men or 35 inches for women

Most people who have obesity meet all three of these diagnostic markers. People who have significantly increased MUSCLE mass, such as performance athletes and bodybuilders, may have a higher BMI without having obesity.

Treatment Options and Outlook

The treatment for obesity is weight loss. Treatment options include lifestyle modifications, BEHAVIOR MODIFICATION THERAPY, medications to suppress appetite, and BARIATRIC SURGERY. Many people experience better results with a combination of treatments; lifestyle modifications are essential for sustained weight management, regardless of other treatments. However, most people who have obesity have tried many weight loss approaches without success.

Noninvasive methods are more likely to succeed for people who have class 1 obesity. The US National Institutes of Health (NIH) recommends aggressive noninvasive treatment for people who have class 2 obesity but who have not yet developed significant co-morbidities (health conditions resulting from and intertwined with obesity). For people who have class 2 obesity and two or more comorbid conditions (such as hypertension and diabetes) and for people who have class 3 obesity, the NIH recommends bariatric surgery. Though bariatric surgery entails significant risks, health experts believe the benefits of extensive weight loss that is possible outweigh the risks of the surgery when body fat percentage exceeds 30 percent (class 3 obesity).

The long-term success of treatment for obesity requires ongoing and continuous management of obesity's numerous and often intertwined causes. For some people weight management remains a lifelong challenge and sometimes a struggle though others are able to achieve and maintain healthy weight.

Risk Factors and Preventive Measures

The key risk factors for obesity are physical inactivity and excessive food consumption. People who are sedentary (get no physical exercise) are at highest risk for obesity. Nutritious eating habits and daily physical exercise are preventive as well as therapeutic. To prevent obesity health experts recommend

- food (CALORIE) intake appropriate for age and physical activity level
- eating foods with high nutrient density, notably fruits, vegetables, whole grains and whole grain products, and low-fat proteins
- minimizing consumption of high-fat foods (such as fast foods and snack items) and empty carbohydrates (such as sodas and sweets)
- a minimum 30 minutes a day of moderate physical exercise such as walking

Preventive efforts are most likely to succeed when all members of the household participate in them.

See also CHILDHOOD OBESITY; CULTURAL AND ETHNIC HEALTH-CARE PERSPECTIVES; EATING DISORDERS; GENERATIONAL HEALTH-CARE PERSPECTIVES; HEALTHY PEOPLE 2010; INSULIN RESISTANCE; LIFESTYLE AND HEALTH; OBESITY AND HEALTH; PEER PRESSURE; SMOKING AND HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

CLINICAL CLASSIFICATIONS OF OBESITY

Body Mass Index (BMI)	Clinical Classification	Health Risk
30 to 34.9	class 1	moderate
35 to 39.9	class 2	serious
40 and above	class 3	severe or morbid

obesity and health Obesity reached the status of health crisis in the United States in the 1990s. In 2005, one third of Americans—nearly 60 million people—weighed 20 percent or more above healthy body weight, the key clinical marker for diagnosing obesity. An equal number were overweight, weighing 5 to 20 percent above healthy body weight. Many health experts believe obesity is as significant a health risk factor as cigarette smoking, complicit in a broad spectrum of health conditions.

HEALTH CONDITIONS IN WHICH OBESITY CAN BE A FACTOR

ATHEROSCLEROSIS	BREAST CANCER
COLORECTAL CANCER	CORONARY ARTERY DISEASE (CAD)
ENDOMETRIAL CANCER	ERECTILE DYSFUNCTION
GALLBLADDER DISEASE	GASTROESOPHAGEAL REFLUX DISORDER (GERD)
HEART FAILURE	INSULIN RESISTANCE
HYPERTENSION	OBSTRUCTIVE SLEEP APNEA
MENSTRUAL DYSFUNCTION	OVARIAN CANCER
OSTEOARTHRITIS	PROSTATE CANCER
POLYCYSTIC OVARY SYNDROME (PCOS)	SEXUAL DYSFUNCTION
STEATOHEPATITIS	type 2 DIABETES

How Obesity Affects the Body and Health

Obesity has numerous negative influences on health. It is the leading cause of HYPERTENSION (high BLOOD PRESSURE) and type 2 DIABETES and is an independent risk factor for the development of ATHEROSCLEROSIS, CORONARY ARTERY DISEASE (CAD), PERIPHERAL VASCULAR DISEASE (PVD), OSTEOARTHRITIS, GALLBLADDER DISEASE, COLORECTAL CANCER, hormone-driven BREAST CANCER, and PROSTATE CANCER. Health risk for these conditions and their complications or consequences increases moderately for overweight and significantly for obesity. In addition to its role as a key risk factor for numerous health conditions, obesity is itself a health condition with significant and potentially fatal consequences when it remains untreated.

Obesity and type 2 diabetes More than 95 percent of people who have type 2 diabetes are overweight and many have obesity. Increased body fat decreases cell sensitivity to INSULIN, which sets in motion a cascade of adaptations that ultimately overwhelm the body's normal metabolic balance. Cells become resistant to insulin (the prediabetes condition INSULIN RESISTANCE), which requires increasingly higher levels of GLUCOSE in the BLOOD circulation to initiate an appropriate insulin response. The high blood glucose levels essentially "burn out" the cells that form delicate nerves and blood vessels, causing them to die. The resulting irreversible damage manifests as PVD and NEUROPATHY.

In an effort to bring blood glucose levels down, the ISLETS OF LANGERHANS in the pancreas, which contain the cells that produce insulin, pump out increasing amounts of insulin. The environment within the body reaches the state of type 2 diabetes when the islet cells can no longer keep pace with the body's demands. The amount of glucose in the blood circulation ultimately reaches levels that cause symptoms such as excessive thirst and URINATION that represent the body's efforts to rid itself of the excessive glucose. Symptoms that reflect damage resulting from elevated blood glucose also occur, such as vision changes, development of cataracts, tingling or loss of sensation in the feet, and wounds that do not heal.

Obesity and cardiovascular disease (CVD) Obesity sets the stage for HYPERLIPIDEMIA, the pathologic circumstance of excessive lipids (fatty acids) in the blood circulation. Hyperlipidemia is the foundation of occlusive forms of CARDIOVASCULAR DISEASE (CVD) such as CAD, atherosclerosis, and CAROTID STENOSIS. Obesity is also the primary cause of hypertension, partly as a consequence of obstructive CVD such as atherosclerosis and partly because the pressure excessive body fat places on the arteries, veins, and organs increases the resistance blood encounters as it flows through the circulation and forces the HEART to work harder to pump blood. The increased workload of the heart may lead to HEART FAILURE.

Obesity and osteoarthritis Excessive body weight places considerable stress on the structures of the musculoskeletal system, most notably the back, hips, knees, ankles, and feet. The CARTILAGE that pads and cushions the joints distorts under such pressure, and over time sustains permanent damage. Physical inactivity exacerbates the situation. Osteoarthritis symptoms dramatically improve with weight loss, however, and much of the temporary damage to the structures of the joints is able to heal.

Obesity and gallbladder disease Gallstones are three times more common in people who have obesity. Lipids and fatty acids in the blood circulation provide the LIVER with a supply of the material it needs to manufacture cholesterol, a key ingredient of BILE. Ironically, rapid weight loss in someone who has obesity (greater than three pounds per week) also triggers formation of gallstones.

Obesity and cancer Rates of certain cancers are significantly higher in people who have obesity. The correlation is strongest for hormonally driven cancers such as prostate cancer in men and breast cancer, OVARIAN CANCER, and ENDOMETRIAL CANCER (cancer of the UTERUS) in women. Many health experts believe obesity is a major risk factor for colorectal cancer, particularly in men, though studies are less conclusive than for obesity's correlation with other cancers.

Obesity as an independent health condition Aside from its role as a contributing factor to numerous health conditions, which doctors call co-morbidity, obesity itself is a disorder with metabolic, cardiovascular, pulmonary, and musculoskeletal symptoms. The presence of obesity alone, setting aside all correlating health conditions, shortens LIFE EXPECTANCY nearly as much as cigarette smoking. People who weigh more than 30 percent above healthy body weight are up to 10 times more likely to die prematurely of any cause. The excessive weight and body mass stresses all structures of the body, pressuring internal organs, including the LUNGS, and affecting their ability to function.

Obesity and Quality of Life

Obesity, notably class 3 (morbid) obesity in which a person weighs 100 pounds or more above healthy weight, has a measurably detrimental effect on QUALITY OF LIFE. This level of obesity presents challenges for finding clothing, seating on airplanes, sitting on chairs, riding in cars, navigating store aisles, and even simply being able to walk to get around for the activities of daily living. These challenges commonly result in social isolation and can be a problem for developing friendships and relationships.

Health conditions that have developed as a consequence of obesity may hinder some weight management efforts, notably physical exercise. It is important to find activities that are enjoyable and to persist in them to the extent that they do not worsen other health conditions. A person who has painful osteoarthritis, for example, may choose to walk for 5-minute periods of time four to six times a day instead of walking for 20 or 30 minutes at a time. The cumulative benefit of the short periods of exercise are as effective and easier to accommodate.

OVERCOMING OBSTACLES

Health conditions that limit mobility may interfere with activities such as grocery shopping, leading to relapses in EATING HABITS. Alternative methods to obtain healthful foods might include hiring a teenage neighbor who can drive to shop on a regular basis or shopping through the online services many grocery stores now offer. For a small fee, such services select the items requested and deliver them to the home.

See also CHILDHOOD OBESITY; DEPRESSION; DIABETES PREVENTION; DIET AND HEALTH; EATING DISORDERS; EXERCISE AND HEALTH; LIFESTYLE AND HEALTH; WEIGHT LOSS AND WEIGHT MANAGEMENT.

S

smoking and health There are no health benefits and numerous health risks from cigarette smoking. In the 1940s few people, including doctors, recognized the magnitude of health risks associated with cigarette smoking. But 20 years later cigarette smoking was a known and publicly identified risk factor for numerous health conditions and the primary cause of HEART disease and LUNG CANCER. In the 1965 cigarette smoking in the United States peaked with about 45 percent of American adults being smokers; by the early 2000s, only 23 percent of American adults smoked. However, that 23 percent represents 48 million people who have significantly increased risk for CARDIOVASCULAR DISEASE (CVD), chronic lung disease, and cancer. Cigarette smoking remains the leading cause of preventable disease in the United States.

PACK YEARS AND DISEASE RISK

One method of representing the amount of cigarette smoke exposure an individual has had is the "pack year." This calculation expresses the number of packs of cigarettes a person smokes each day times the number of years the person has smoked. A person who has smoked for 10 pack years may have smoked half a pack a day for 20 years, one pack a day for 10 years, or two packs a day for five years. The higher the number of pack years, the greater exposure and more significant the risk of pulmonary and cardiovascular disease.

How Smoking Affects the Body and Health

Cigarette smoking affects every cell in the body beginning within seconds of the first inhalation from a cigarette. NICOTINE contracts BLOOD vessels, increases HEART RATE, raises BLOOD PRESSURE, and activates neurotransmitters in the BRAIN that result in CENTRAL NERVOUS SYSTEM stimulation to produce a combined sense of exhilaration and alertness. With each inhalation of cigarette smoke, tar makes its way to the delicate alveoli deep within the LUNGS, clogging them and preventing them from exchanging oxygen. Other chemicals in the smoke irritate the bronchi, causing an increase in mucus production and narrowing of the bronchial openings. Carbon monoxide beats out oxygen to bind with HEMOGLOBIN in the red blood cells (erythrocytes), cutting by up to 60 percent the amount of oxygen each breath carries into the blood circulation. The combined effects of these actions and the chemicals that enter the bloodstream affect cellular METABOLISM in countless ways. Dozens of these chemicals are carcinogenic; they cause cells within the body to develop into cancers. Some of the effects linger for hours after the cigarette and compound with further smoking.

Cigarette smoking and CVD The leading health consequence of cigarette smoking is CVD. Repeated exposure to nicotine causes permanent changes in the cells that form the lining of the arteries, making the arteries vulnerable to ATHEROSCLEROTIC PLAQUE deposits and, over time, ATHEROSCLEROSIS, CORONARY ARTERY DISEASE (CAD), and PERIPHERAL VASCULAR DISEASE (PVD). Persistent nicotine exposure also causes the arteries to stiffen and lose FLEXIBILITY. These changes lead to HYPERTENSION (high blood pressure) and increased risk for HEART ATTACK and STROKE. The strain on the heart can eventually cause HEART FAILURE.

Cigarette smoking and cancer The primary form of cancer associated with cigarette smoking is lung cancer. However, cigarette smoking increases the risk for various forms of cancer, including oral cancer, laryngeal cancer, ESOPHAGEAL CANCER, PANCREATIC CANCER, BLADDER CANCER, PROSTATE CANCER,

BREAST CANCER, RENAL CANCER, STOMACH CANCER, and LIVER CANCER. The burning of a cigarette releases smoke that contains more than 4,000 chemicals, dozens of which are known carcinogens (substances that cause cancer).

CARCINOGENS IN CIGARETTE SMOKE

acrolein	acrylonitrile
aminobiphenyl	aromatic amines
aromatic nitrohydrocarbons	arsenic
benzene	benzofluoranthene
benzopyrene	butadiene
cadmium	chromium
chrysene	crotonaldehyde
dimethylhydrazine	dibenzacridine
dibenzanthracene	dibenzocarbazole
dibenzopyrene	ethylcarbamate
formaldehyde	hydrazine
hydrocarbons	lead
methylamine	methylchrysene
naphthylamine	nickel
nitropropane	nitrosamines
nitrosonomicotine	phenols
polonium-210 (radon)	quinoline
tar	toluidine
urethane	vinyl chloride

Cigarette smoking and chronic pulmonary conditions Cigarette smoking is the primary cause of numerous chronic pulmonary conditions, including CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD), chronic BRONCHITIS, and nonallergic ASTHMA. The damage that results from COPD is irreversible and progressive, often leading to permanent disability.

Cigarette smoking and healing The changes that take place in the cells with cigarette smoking slow cellular metabolism, limiting the ability of cells to grow and divide. These functions are essential for HEALING after injury or surgery. As well, lungs damaged by cigarette smoking are unable to deliver adequate oxygen to the blood circulation, restricting a fuel source necessary for cell function. The effects of cigarette smoking on healing are so significant that most surgeons will not perform elective (nonemergency) operations on people who smoke. It is necessary to be smoke free for two to four weeks to mitigate enough of smoking's deleterious action on cellular function to allow effective healing.

Cigarette smoking, fertility, and pregnancy Cigarette smoking affects sperm production in men and OVULATION in women. Smoking during PREGNANCY limits the amount of oxygen the developing fetus receives, affecting fetal growth and development. The babies of women who smoke during pregnancy tend to be 10 to 20 percent smaller at birth than the babies of women who do not smoke. Low birth weight is a health risk for the infant.

Smoking and Preventable Disease

Nearly all of the health consequences associated with cigarette smoking are preventable by not smoking. People who never smoke enjoy the strongest preventive benefit. People who smoke and quit can, over time, restore their health risk for many conditions to near normal. Health conditions such as COPD, lung cancer, laryngeal cancer, and bladder cancer are rare in nonsmokers. Other factors such as EATING HABITS and physical inactivity contribute to CVD, though not smoking removes a significant factor from an individual's health risk profile.

See also ANTISMOKING EFFORTS; ENVIRONMENTAL CIGARETTE SMOKE; ERYTHROCYTE; LIFESTYLE AND HEALTH; NEUROTRANSMITTER; NICOTINE REPLACEMENT; SMOKING CESSATION; TOBACCO USE OTHER THAN SMOKING.

smoking cessation Efforts to stop smoking. Tobacco contains NICOTINE, the addictive quality of which is comparable to that of HEROIN. As well, cigarette smoking becomes a compelling behavioral element of daily life. Most smokers who attempt to quit make numerous efforts before succeeding for the long term and the risk for relapse remains high for years. Of the 1.8 million American smokers who quit every year, 30 percent remain smoke free for one year.

Several medical interventions can help to smokers break the grip of nicotine, including NICOTINE REPLACEMENT products (such as chewing gums, transdermal patches, inhalers, and nasal sprays) and the prescription medication bupropion (Zyban), which appears to diminish the desire to smoke. Nonmedical interventions include HYPNOSIS and BEHAVIOR MODIFICATION THERAPY. Many smokers are more successful with a combination of methods than with a single approach; those who smoke

more than 25 cigarettes a day generally benefit more from a structured smoking cessation program with ongoing support and encouragement from a therapist or through a support group.

TIPS FOR SUCCESSFUL SMOKING CESSATION

- Prepare to stop smoking by eliminating all items associated with smoking such as lighters, ashtrays, and cigarettes.
- Identify places and circumstances where smoking is likely to be irresistible and plan alternatives.
- Purchase NICOTINE REPLACEMENT products before quitting and place them in former smoking places, such as in the bathroom, kitchen, and car.
- Plan a system of self-reward for success in meeting short-term goals.
- Arrange with someone to be available around the clock to call when the urge to light up becomes intense.
- Use stress management techniques such as meditation, yoga, and physical exercise to unwind and relax.

The effect of nicotine remains active in the body for about 20 minutes after smoking a cigarette. For many smokers the time between the last cigarette and what would have been the next cigarette is the most difficult, as the body exerts its demand for the next DOSE of nicotine. After 72 hours the nicotine urge subsides considerably. Each day, week, and month without smoking lessens the body's sense of nicotine dependence. About 75 percent of people who make it one month smoke free are able to stay smoke free for one year. Each year of remaining smoke free increases the likelihood of long-term smoking cessation. It is important to take setbacks in stride, identify and eliminate the trigger for the setback, and quickly resume smoking cessation efforts.

See also ANTISMOKING EFFORTS; SMOKING AND CARDIOVASCULAR DISEASE; SMOKING AND HEALTH; TOBACCO USE OTHER THAN SMOKING.

T–U

tobacco use other than smoking Forms of tobacco such as chewing tobacco and smoking cigars. Tobacco use other than cigarette smoking is the primary cause of oral cancers (cancers that involve structures of the MOUTH). The two primary forms of tobacco use other than cigarettes are cigars and smokeless tobacco.

Cigar and Pipe Smoking

Cigar and pipe smoke contains many of the same chemicals and carcinogens as cigarette smoke. Because cigar and pipe smokers hold the smoke in their mouths rather than inhaling it, the structures of the mouth have intense exposure to these chemicals. Long-term exposure to tobacco smoke is detrimental to the gums and TEETH and increases the risk for CARDIOVASCULAR DISEASE (CVD).

Though the risk of LUNG CANCER from smoking cigars or pipes is less than that from smoking cigarettes, it is notably higher than for people who do not smoke at all and in people who smoke three or more cigars a day. People who regularly smoke cigars also have higher risk for PANCREATIC CANCER, laryngeal cancer, and ESOPHAGEAL CANCER. The most significant cancer risks from cigar smoking are cancers of the lips, tongue, cheeks, soft palate (roof of the mouth), floor of the mouth, and gums.

Smoking two to three cigars or more a day raises the risk for CVD nearly as much as cigarette smoking. The NICOTINE in tobacco becomes rapidly absorbed into the BLOOD circulation through the mucous membranes in the mouth. Nicotine stimulates the smooth MUSCLE that makes up the walls of the arteries, causing the arteries to stiffen. Chronic exposure to nicotine also alters the structure of the muscle fibers in the arterial walls, reducing their FLEXIBILITY. These changes cause HYPERTENSION (high BLOOD PRESSURE). The changes to the arterial wall's structure also facilitate the accumulation of arterial plaque and atherosclerotic deposits, leading to ATHEROSCLEROSIS and increasing the risk for CORONARY ARTERY DISEASE (CAD).

Smokeless Tobacco

It is a common misperception, particularly among young people, that smokeless tobacco is safe because there is no smoke involved with its use. This is not true. Smokeless tobacco contains nicotine, which is highly addictive. It can be as difficult to quit using smokeless tobacco as it is to stop smoking. A pinch or dip of smokeless tobacco contains as much nicotine as three cigarettes. Forms of smokeless tobacco include snuff, which is powdery, and chewing tobacco (plugs, twists, and loose leaf).

Smokeless tobacco is particularly damaging to the teeth and gums. After only a few years of regular use, the gum tissue may become structurally unstable, unable to support the teeth. Tooth loss may be unpreventable in such circumstances. The irritation of the tobacco against the gums and cheeks also causes sores that can be painful or can further erode the tissue around the base of the teeth. Tobacco juice permanently stains the teeth yellow or brown and erodes the enamel outer layer, increasing the risk for DENTAL CARIES (cavities) and weakening the teeth.

About four times the concentration of nicotine enters the blood circulation from smokeless tobacco as from cigarette smoking. Nicotine that enters the blood circulation by being absorbed through the tissues of the mouth has the same negative effects on the blood vessels as nicotine that enters the blood circulation through the

LUNGS, raising the risk for atherosclerosis and CAD with prolonged use. As well, smokeless tobacco contains carcinogens that release into the mouth and is the leading cause of oral cancers. Doctors diagnose 30,000 people with oral cancers due to smokeless tobacco use each year in the United States; about 8,000 Americans die each year from such oral cancers.

CARCINOGENS IN SMOKELESS TOBACCO

acetaldehyde	arsenic
benzopyrene	cadmium
crotonaldehyde	formaldehyde
hydrazine	nitrosamine acids
polonium-210 (radon)	tobacco-specific nitrosamines (TSNAs)
volatile aldehydes	
volatile nitrosamines	

See also CARCINOGEN; HALITOSIS; SMOKING AND CANCER; SMOKING AND HEALTH; SMOKING CESSATION.

triceps skinfold A measure of the thickness of a fold of SKIN at the triceps (MUSCLE at the back of the upper arm), which indicates BODY FAT PERCENTAGE. Triceps skinfold thickness is easy for doctors, nutritionists, and fitness professionals to measure as a means of monitoring loss of body fat. A tensioned caliper, placed over a segment of pinched skin at the triceps, measure the skinfold thickness in millimeters. The thickness value corresponds roughly to the body fat percentage. For example, a triceps skinfold measurement of 10 millimeters (mm) corresponds to approximately 10 percent body fat; of 35 mm to approximately 35 percent body fat. The triceps skinfold measurement may also serve as an indicator for adequate nutrition in infants and young children, with less than 5 mm (5 percent body fat) indicating insufficient nutrition.

See also BODY MASS INDEX (BMI); UPPER ARM CIRCUMFERENCE; WAIST CIRCUMFERENCE; WAIST TO HIP RATIO.

upper arm circumference A measurement of the distance around the center of the upper arm, which serves as an approximate measure of LEAN MUSCLE MASS. Upper arm circumference, also called mid-upper arm circumference (MUCA), is one method to estimate appropriate nutrition. The muscles store protein, thus measuring the size of muscles provides an approximation of the body's protein supply. In undernutrition and MALNUTRITION MUSCLE size shrinks because the body metabolizes protein stores to generate energy. Overnutrition (overweight and OBESITY) results in exaggerated muscle size as a consequence of high amounts of fat in the muscle fibers. RESISTANCE EXERCISE such as weightlifting enlarges the upper arm muscles, which can make upper arm measurement less accurate as an assessment of lean muscle mass.

UPPER ARM CIRCUMFERENCE AND HEALTH

Measurement (centimeters)	Health Risk Correlation
<16	MALNUTRITION
16.1 to 18.5	increased risk for undernutrition
18.6 to 22	no increased health risk
22.1 to 25	overweight, moderate health risk
> 25	OBESITY, significant health risk

See also BODY MASS INDEX (BMI); TRICEPS SKIN FOLD; WAIST CIRCUMFERENCE; WAIST TO HIP RATIO; WEIGHT LOSS AND WEIGHT MANAGEMENT.

W

waist circumference The distance measured around the waist. Doctors define the waist as the imaginary line that circles the body between the umbilicus (belly button) and the crest of the hip bones. Healthy waist circumference is less than 35 inches for a woman and less than 40 inches for a man, regardless of age. Waist circumference is an important measure of health risk for conditions such as OBESITY, INSULIN RESISTANCE, type 2 DIABETES, and forms of CARDIOVASCULAR DISEASE (CVD) such as HYPERTENSION (high BLOOD PRESSURE), HYPERLIPIDEMIA, ATHEROSCLEROSIS, and CORONARY ARTERY DISEASE (CAD). Excessive waist circumference also dramatically increases risk for HEART ATTACK.

Though waist circumference alone increases the risk for health conditions, the risk compounds when it occurs in combination with elevated BODY MASS INDEX (BMI). Health risk rises moderately when BMI reaches 25 and significantly when BMI reaches 30. In combination with waist circumference that exceeds 35 inches for a woman or 40 inches for a man, health risk jumps to the next level. Other risk factors for CVD, such as cigarette smoking and physical inactivity, further increase the likelihood for heart disease, heart attack, and STROKE. Weight loss sufficient to decrease waist circumference also decreases BMI, improving the health risk.

Waist circumference that exceeds 35 inches for women or 40 inches for men when body weight is within the range of healthy (BMI of 18.5 to 24.9) indicates a body fat distribution pattern of ABDOMINAL ADIPOSITY, which reflects increased risk for heart attack and CVD even when no other risk factors for heart disease are present. Doctors recommend modest weight loss (5 to 10 percent), with emphasis on increased physical activity, to reduce waist circumference.

See also HEALTH RISK FACTORS; WAIST TO HIP RATIO; WEIGHT LOSS AND WEIGHT MANAGEMENT.

waist to hip ratio The proportion between the distance around the waist and the distance around the hips (WAIST CIRCUMFERENCE divided by hip circumference). A waist to hip ratio of 0.9 in men and 0.8 in women indicates an "apple" body shape, which reflects an elevated body fat percentage, heralds an increased risk for CARDIOVASCULAR DISEASE (CVD) and HEART ATTACK in particular. The higher the waist to hip ratio, the greater the risk.

WAIST TO HIP RATIO AND HEALTH RISK

Health Risk	Men	Women
healthy, no increased risk	0.89 or less	0.79 or less
moderate to significant	0.9 or greater	0.8 or less

WAIST CIRCUMFERENCE, BODY MASS INDEX (BMI), AND HEALTH RISK DUE TO WEIGHT

Health Risk	Moderate	Significant	Severe
BMI overweight (25 to 29.9)	X		
waist > 35 inches/40 inches	X		
BMI overweight plus waist > 35/40 inches		X	
BMI OBESITY class 1 (30 to 34.9)		X	
BMI obesity class 1 plus waist > 35/40 inches			X

See also ABDOMINAL ADIPOSITY; BODY MASS INDEX (BMI); BODY SHAPE AND CARDIOVASCULAR DISEASE; UPPER ARM CIRCUMFERENCE.

weight loss and weight management The approaches and methods to lose excessive weight and maintain healthy weight after weight loss. Two thirds of Americans weigh more than is healthy, with a corresponding increase in weight-related health conditions such as HYPERTENSION (high BLOOD PRESSURE), type 2 DIABETES, OSTEOARTHRITIS, ATHEROSCLEROSIS, and CORONARY ARTERY DISEASE (CAD). Americans also spend tens of billions of dollars each year on diet programs, books, diet aids, and other weight-loss products. Yet the premise of weight loss and weight management is fairly simple: eat less and exercise more as a matter of lifestyle.

Losing Weight

A weight loss approach that balances decreased food intake and increased exercise can provide steady, sustainable results. Health experts recommend a rate of nonsurgical weight loss that targets no more than a 10 percent drop in weight over no less than six months for optimal success in keeping the weight off long term. Short-term weight loss goals help monitor progress and establish a sense of success. Methods for weight loss include lifestyle modifications, BEHAVIOR MODIFICATION THERAPY, medication therapy, and BARIATRIC SURGERY.

Lifestyle modifications: eating habits and exercise Lifestyle is the cornerstone of weight management. Many people achieve greater success with their weight loss efforts when they join programs that incorporate nutritional control (such as prepared meals or stringent menus) and structured physical exercise (such as group classes). However, fad diets that promise rapid weight loss generally do not produce sustainable results.

It is important for people who need to lose weight to understand portion sizes, NUTRIENT DENSITY, NUTRITIONAL NEEDS, and nutritional food choices that are also palatable. This understanding is essential for incorporating healthy EATING HABITS into long-term lifestyle modifications. Unless under a doctor's supervision and guidance, daily CALORIE intake should never drop below 1,200 calories for women and 1,600 calories for men. Calorie intake below these levels activates the body's starvation mechanisms, which result in slower METABOLISM and efforts to conserve energy (calories). Daily exercise is essential to increase the body's energy expenditure. During weight loss efforts, increased activity and decreased food consumption combine for the most efficient results.

30 MINUTES A DAY = 15 POUNDS A YEAR

One pound of fat is the equivalent of 3,500 calories. Physical exercise at the minimum recommended level of 30 minutes daily typically consumes 150 calories a day. This adds up to nearly 1½ pounds a month, or 15 pounds a year, lost through exercise alone.

Behavior modification therapy Behavior modification therapy may incorporate techniques such as taking smaller portions with the understanding that one can have more if still hungry, extending consumption of a meal over a certain period of time to encourage a slower pace of eating, eating only at the table without reading or watching television, keeping a food and exercise journal, scheduling exercise "appointments," and shopping after eating and only from a list.

Medication therapy Prescription APPETITE suppressants can help people follow portion size and eating recommendations to reduce the amount of calories they consume. Medications tend to become less effective over time. Researchers are uncertain whether this is an issue of physiologic tolerance (the body becomes resistant to the medication's effect) or a matter of becoming accustomed to the medication and more able to overcome its effect. Medication may be an appropriate treatment for people who have a BODY MASS INDEX (BMI) between 30 and 34.9 (class 1 OBESITY) and who have been unsuccessful with efforts to lose weight. The medications to suppress appetite may have significant side effects or DRUG interactions.

Over-the-counter (OTC) diet medications often contain CAFFEINE or a decongestant such as pseudoephedrine. These drugs may mildly suppress the appetite though their long-term use may result in side effects such as agitation and PALPITATIONS. OTC diet products generally provide no greater benefit than diet and exercise alone.

MEDICATIONS TO SUPPRESS APPETITE

Medication	Actions	Possible Side Effects
orlistat (Xenical)	blocks intestinal absorption of fat	frequent or uncontrollable bowel movements deficiency of fat-soluble vitamins (A, D, E, and K)
phentermine (Fastin)	CENTRAL NERVOUS SYSTEM stimulant increases NOREPINEPHRINE levels in the BRAIN, which suppresses the APPETITE and HUNGER centers	dependency PALPITATIONS insomnia DRUG INTERACTION with monoamine oxidase inhibitor (MAOI) antidepressants
sibutramine (Meridia)	increases norepinephrine and serotonin levels in the brain, an action that suppresses the appetite and hunger centers and elevates mood	serotonin syndrome drug interaction with narcotic analgesics, selective serotonin reuptake inhibitor (SSRI) antidepressants, and MAOI antidepressants

Bariatric surgery Weight loss surgery is a drastic measure that becomes a treatment option when an individual's weight exceeds 100 pounds over healthy weight (class 3 obesity) or otherwise directly and immediately threatens health. Most bariatric surgery operations either restrict the size of the STOMACH to limit the volume of consumed food or alter the flow of ingested food to curtail absorption. Surgery for weight loss has numerous risks and potential complications, though may be the therapeutic approach that succeeds for people who have been otherwise unable to reach a healthier weight.

HEALTH BENEFITS OF WEIGHT LOSS

- decrease OSTEOARTHRITIS symptoms
- improve INSULIN sensitivity
- relieve OBSTRUCTIVE SLEEP APNEA
- improve type 2 DIABETES
- increase energy and mobility
- reduce risk for CARDIOVASCULAR DISEASE (CVD)
- relieve chronic BACK PAIN
- improve HYPERLIPIDEMIA
- improve HYPERTENSION
- improve LIBIDO and sexual function
- improve self-esteem
- improve FERTILITY
- reduce risk for cancer
- reduce risk for type 2 diabetes
- relieve GASTROESOPHAGEAL REFLUX DISORDER (GERD)

Maintaining Healthy Body Weight

Weight loss that is gradual and steady generally results from incorporating lifestyle changes that will support sustained weight management. Even small progress makes a measurable difference in health and well-being.

Social and family support Encouragement and support for weight loss and weight management from family and friends is crucial for long-term success, though is often a complex dynamic. Some people find themselves alone in their weight loss efforts because other family members do not want to make the same changes in their own eating habits and physical activity. Other people are able to make weight loss and weight management a family endeavor or to join with friends to support and encourage one another. Positive reinforcement for achievements, however small, is far more effective than criticism.

Relapse and weight gain Relapses of regained weight are common and disheartening. However, the quicker a person recognizes that his or her weight is slipping back toward obesity the easier it is to stop the slide and return to the treatment methods that were effective. Unfortunately many people tend not only to regain lost weight but also to gain additional weight. Such a rebound or "yo-yo" effect is especially detrimental to health. It is important to get back on track with eating habits and exercise as quickly as possible to halt weight gain before it becomes overwhelming to confront.

See also DIET AND HEALTH; EATING DISORDERS; EXERCISE AND HEALTH; OBESITY AND HEALTH.

SUBSTANCE ABUSE

Substance abuse is the use of any DRUG*, including* ALCOHOL*, or other psychoactive substances in ways that are harmful to a person or others whom the person's actions may affect. Health-care practitioners who provide care for people who have substance abuse problems, alcohol or drug* DEPENDENCE*, and* ADDICTION *may be physicians (MDs or DOs), psychiatrists (physicians who specialize in psychiatric disorders), psychologists (PhDs), social workers (LSWs), and clinical registered nurse practitioners (CRNPs). Practitioners may be certified substance abuse professionals (SAPs), designating that they have additional education and experience in treating substance abuse (including* ALCOHOLISM*).*

This section, "Substance Abuse," presents an overview discussion of the health implications of substance abuse and alcoholism and entries about substances of abuse, health risks related to substance abuse, and treatment for substance abuse.

From Tonic to Toxin: Opium's Odyssey

Many substances currently restricted because of their high potential for abuse were once in common use. For centuries cultures around the world used opium, the dried sap from the poppy plant, *Papaver somniferum*, to relieve PAIN, induce sleep, and provide INTOXICATION. In 1805 a young pharmacist's assistant, Freidrich Wilhelm Adam Serturner (1783–1841), isolated morphine, opium's most potent ingredient, from opium; 90 years later chemists at the Bayer Company created HEROIN from morphine. For the next decade the most common use of heroin was to treat morphine addiction—clearly a circumstance, in retrospect, of leaping from the frying pan into the fire.

By 1913 the Bayer Company stopped producing heroin, and in the 1920s opium and heroin became illegal in the United States. Federal law regulated the manufacture, sale, and possession of morphine and other medicinal OPIATES. Nonetheless heroin continued to make its way into the United States, and in 1970 its abuse peaked with more than 750,000 Americans addicted. Perhaps not so coincidentally the US Congress passed the Controlled Substances Act, the first comprehensive classification and enforcement legislation for drugs, in the same year. Through concerted legal, social, and medical efforts heroin abuse declined significantly over the following 30 years, and in 2004 the US Substance Abuse and Mental Health Administration (SAMHA) estimated 166,000 people actively using heroin.

Opiates, and in particular morphine and its direct derivatives, remain the mainstay of analgesia (pain relief) in medical treatment though under tight regulatory control. Tens of millions of Americans use opiates for effective pain management. However, PRESCRIPTION DRUG ABUSE of opiate NARCOTICS such as hydromorphone, hydrocodone, oxycodone, and codeine becomes problematic for about four million of them.

Health Implications of Substance Abuse

Addiction is a condition that develops over time, regardless of the substance or behavior that is the source of the addiction. Social factors compound the health issues of addiction; many people are afraid or reluctant to acknowledge a possible addiction for fear of repercussions in all areas of their lives. Despite advances in understanding addiction in recent years, the perception remains that addiction is a matter of insufficient willpower. However, addiction arising from substance abuse (whether alcohol, NICOTINE, illicit drugs, or prescription drugs) represents a complex entanglement of physiologic, psychologic, and social factors. Many people abuse multiple substances though have a primary substance of abuse.

DRUG SLANG

Drug Name	Slang Names
ALKYL NITRITES	rush, locker room, rave, poppers, snappers
AMPHETAMINES	speed, go-pill, upper
BARBITURATES	yellow jackets, reds, blues, rainbows, downers, barbs, goofballs
COCAINE	coke, snow, flake, blow, big C, lady, nose candy, white, party favors
DEXTROMETHORPHAN	DXM, skittles, candy, c-c-c, dex, DM, Drex, red devils, tussin, velvet
FLUNITRAZEPAM (Rohypnol)	roofies, rophies, roach, rope, forget-me pill
GAMMA HYDROXYBUTYRATE (GHB)	liquid ecstasy, soap, easy lay, vita-G, Georgia home boy
HEROIN	smack, horse, brown sugar, junk, black tar, big H, bag
KETAMINE	special K, vitamin K, super K, keets
lysergic acid diethylamide (LSD)	acid, blotter, trip, hit, sugar cube, microdot, tab, purple haze
marijuana	pot, weed, reefer, mary jane, aunt mary, boom, kif, skunk, herb, dope, gangster
METHAMPHETAMINE	speed, crank, crystal, ice, glass, meth, crystal meth
METHYLENEDIOXYMETHAMPHETAMINE (MDMA)	XTC, X, hug drug, ecstasy, ecstacy
PHENCYCLIDINE (PCP)	angel dust, ozone, wack, rocket fuel, crystal supergrass, embalming fluid, killer joint

Often the break from the addictive behaviors occurs as a consequence of intervention, either by family members and friends or through legal processes such as court-imposed sentencing to a substance abuse program. Unfortunately, such intervention all too often comes at the cost of injury to self or others. Alcohol is a factor in more than half of MOTOR VEHICLE ACCIDENTS in the United States. Other substances that alter perception, judgment, and reaction time further contribute to traffic accidents, which are the leading cause of accidental injury and death. These substances include CANNABIS products (marijuana, hashish, hash oil), as well as STIMULANTS, BARBITURATES, BENZODIAZEPINES, and HALLUCINOGENS.

Two thirds of new HIV/AIDS INFECTION among women in the United States result directly or indirectly from injected drug use: either the woman herself injects illicit drugs or has sexual partners who inject illicit drugs. Intravenous drug use is also the leading means of transmitting infection with HEPATITIS B, hepatitis C, and hepatitis D. Intravenous drug users face numerous other risks including ENDOCARDITIS (bacterial infection of the HEART valves), damaged and destroyed veins, cellulitis (infection of the skin and underlying tissue), MALNUTRITION, and poisoning from the unknown ingredients illicit drugs contain as fillers.

Special Risks: Substance Abuse During Pregnancy

Substance abuse during PREGNANCY poses unique risks for the developing FETUS, which may experience health crises at birth and lifelong health consequences. Among the most toxic substances of abuse is alcohol, which is teratogenic at nearly every stage of pregnancy. FETAL ALCOHOL SYNDROME

(FAS) is the most severe complication of maternal alcohol use during pregnancy. FAS may involve significant physical BIRTH DEFECTS, BRAIN damage, developmental delays, LEARNING DISORDERS, and psychologic conditions.

Infants of women who are addicted to drugs are born addicted themselves, requiring intensive medical care after birth to wean them from the drugs and restore normal body functions. These infants are also often born prematurely, further compromising their health and well-being. Though the teratogenic risks of drugs such as heroin and COCAINE remain unclear, long-term health problems and learning disabilities later in childhood are common.

Babies born to women who smoke cigarettes are characteristically of small birth weight, which researchers believe results from insufficient oxygen in the mother's BLOOD circulation. They also have high risk for failure to thrive, a potentially lethal health circumstance in which the infant does not grow and develop normally but for no discernible medical reasons. Such infants require diligent care and frequent medical attention, and are more vulnerable to infection and illness.

Advances in Knowledge and Treatment

Discovery of opiate receptors in the early 1970s was a huge leap forward in understanding how narcotics work in the brain. Subsequent advances allowed researchers to identify the roles of other neuroreceptors and neurotransmitters and to discover alterations in brain function that occur with specific drugs. Psychiatric disorders also play roles in susceptibility to addiction.

Some research has shown that more than 80 percent of people diagnosed with SCHIZOPHRENIA are also heavy cigarette smokers—addicted to nicotine—have other substance abuse problems or addictions. Researchers do not know whether the addictions increase susceptibility for psychiatric illness or psychiatric illness increases vulnerability for addictions.

The multiplicity of factors that contribute to addiction make its treatment all the more difficult. Of the 20 million Americans who have substance abuse or addiction problems, fewer than 4 million seek treatment. New medications that target specific neuroreceptors have vastly improved symptom relief during DETOXIFICATION and help maintain SOBRIETY after withdrawal for many people. Integrated efforts to educate students and employees about the dangers of substance abuse, coupled with mandatory drug testing in a growing number of environments, appear to have significantly reduced substance abuse in certain settings. Focused therapy that helps people learn new behaviors (BEHAVIOR MODIFICATION THERAPY) and gain insight into the reasons they abuse drugs and alcohol (COGNITIVE THERAPY) seems to be improving the success rate for maintaining sobriety. As well, pharmacologic research is producing new kinds of narcotics that can target specific neuroreceptors in ways that provide therapeutic action (such as pain relief) with low risk for addiction.

A

addiction A pattern of lifestyle that revolves around obtaining and using drugs. The behaviors of this pattern are compulsive and difficult to resist or overcome, particularly when there is physical DRUG DEPENDENCE. However, addiction can occur with nearly any substance (such as drugs, ALCOHOL, and tobacco) or behavior (such as gambling) that a person feels he or she cannot live without and is willing to take substantial risks to keep the substance or behavior part of everyday life. For most people addiction is a chronic condition for which successful treatment often requires ongoing diligence, participation in SUPPORT GROUPS, and PSYCHOTHERAPY.

Numerous health complications are associated with addiction. Key among them are HEPATITIS and HIV/AIDS among people who inject drugs using shared needles and paraphernalia. MALNUTRITION is common among people who have addictions to alcohol, HEROIN, COCAINE, AMPHETAMINES, and METHAMPHETAMINE. Prime health risks associated with the leading addiction in the United States, cigarette smoking, include CARDIOVASCULAR DISEASE (CVD) and LUNG CANCER.

SUBSTANCES FOR WHICH ADDICTION IS MOST COMMON

ALCOHOL	AMPHETAMINES
BARBITURATES	BENZODIAZEPINES
CANNABIS compounds	COCAINE
DESIGNER DRUGS	HALLUCINOGENS
inhalants	METHAMPHETAMINE
methylphenidate	NICOTINE
OPIATES	organic solvents

Symptoms and Diagnostic Path

Symptoms of addiction are often apparent to family members and friends long before the person who has the addiction recognizes them. Denial of addiction is itself a key symptom. Specific symptoms of addiction vary with the substance that is the source of the addiction and may cover a broad range of physiologic and psychologic characteristics. General symptoms of addiction may include

- agitation or anxiety
- obsessive interest in maintaining or obtaining access to the substance or behavior
- loss of interest in work, family, and social activities
- isolation from others
- dramatic change in physical appearance, such as continuously runny NOSE, bloodshot eyes, or weight loss

Diagnosis of addiction is a complex process that often includes input from a physician, a psychologist or psychiatrist, and a substance abuse specialist. Though BLOOD and URINE tests may provide evidence that a particular substance is in the body, such test results alone do not establish a diagnosis of addiction. The diagnostic path includes physical and psychologic examinations that look for indications of substance abuse, such as needle tracks (injected drugs) or rotted TEETH (methamphetamine), and behaviors that suggest addiction (most possessions have disappeared, poor PERSONAL HYGIENE, fired from multiple jobs or not able to get a job, frequent arrests or other legal problems).

Treatment Options and Outlook

There are numerous approaches to treatment for addiction, most of which have short-term and long-term components. The treatment approach must meet the specific needs of the individual as

well as address the physiologic and psychologic aspects of the substances to which the person has addictions. In the short term, SUBSTANCE ABUSE TREATMENT may require intensive psychologic support and therapy through an outpatient or inpatient substance abuse treatment program.

Treatment may involve medical care for symptoms of WITHDRAWAL SYNDROME resulting from drug dependence, such as NICOTINE REPLACEMENT patches for tobacco dependence, METHADONE or BUPRENORPHINE for opiate dependence, and disulfiram for alcohol dependence. Medication therapy may also focus on treating underlying or accompanying psychologic disorders such as DEPRESSION (ANTIDEPRESSANT MEDICATIONS) and anxiety (ANTIANXIETY MEDICATIONS). Treatment programs typically also include intensive psychotherapy, BEHAVIOR MODIFICATION THERAPY, COGNITIVE THERAPY, group therapy, and peer support. These approaches attempt to help people understand their motivations for seeking the effects of the substance of abuse, the behaviors they indulge in to achieve the substance, and the ways in which they can replace those behaviors with others that support nondrug-seeking behaviors.

Relapses are common among people who have addictions. Once established, an addiction remains a powerful compulsion even with treatment and methods to mitigate its strength. Absolute avoidance of the substance or behavior (abstinence) is crucial; most addiction experts agree that people who have addictions cannot experience "just a little" of the addiction's source without succumbing again to the addiction. Though researchers do not fully understand the complexity of addiction's mechanisms, they do know that even small exposure to the source can reactivate the addiction. Long-term REMISSION requires persistence and determination in combination with a strong support network of family, friends, and health-care providers.

Risk Factors and Preventive Measures

Multiple factors contribute to addiction. Among the key risks are

- underlying psychologic conditions such as depression, ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD), and POST-TRAUMATIC STRESS DISORDER (PTSD)
- intense feelings of anxiety, loneliness, and loss
- PEER PRESSURE
- family history of ALCOHOLISM or substance abuse

Though genetic factors likely exist that contribute to an individual's vulnerability to addiction, researchers believe such factors are multiple and affect numerous processes within the body. As well, some drugs have higher potential for addiction, notably those that produce an intense response to taking them. Such drugs include methamphetamine, heroin, and cocaine.

It often seems, to those outside looking in at addiction, that the simple solution to preventing addiction is making the choice not to use drugs or alcohol. This is an effective solution in many circumstances; the person who is able to avoid the substance does not develop addiction to substances if not taking them. However, the health condition of addiction is complex; one of its most destructive features is its ability to impair a person's capability to make such choices. The consequences of addiction are often severe yet do not deter the pursuit of the addiction's source. The most effective prevention efforts are those that combine education about substance abuse and its negative health effects with measures to help people choose not to use substances of abuse the first time.

See also GENERALIZED ANXIETY DISORDER (GAD); ILLICIT DRUG ABUSE; NALTREXONE; OBSESSIVE–COMPULSIVE DISORDER (OCD); PRESCRIPTION DRUG ABUSE; SMOKING CESSATION; SCHEDULED DRUG; SUBSTANCE ABUSE PREVENTION; TOLERANCE.

aerosols and glues See ORGANIC SOLVENTS.

alcohol In the context of health and substance abuse a fermented or distilled beverage containing ethanol (also called ethyl alcohol) that, when ingested, has numerous effects on the body, ranging from mild relaxation to INTOXICATION. Alcohol consumption is legal though regulated in the United States by federal and state laws and prohibited by minors (those under age 21). Each state establishes the laws and regulations that govern its alcohol sales. However, access to alcohol is such that underage alcohol consumption is a significant

health and social problem. In the United States, alcohol is a factor in more than one third of MOTOR VEHICLE ACCIDENTS. Long-term alcohol abuse contributes to numerous health conditions including permanent birth defects in children exposed to alcohol during fetal development (FETAL ALCOHOL SYNDROME). Alcohol is the most commonly abused DRUG in the United States.

Alcoholic Beverages

From the perspective of intoxication, a drink is merely the vehicle that carries alcohol into the body. The alcohol in a distilled beverage such as gin is no different from the alcohol in beer or wine. What does differ is the concentration of alcohol within the drink. A distilled drink may contain 40 percent alcohol (represented as "80 proof" on the label); a beer is usually 4 percent and wine is 10 to 14 percent. Thus a 1-ounce shot of distilled spirits, 12-ounce glass of beer, and 5-ounce glass of wine all contain roughly the same amount of alcohol. Each of these is a "standard" drink for purposes of assessing alcohol consumption. Alcohol contains 7 calories per gram, 100 to 150 calories per standard drink. Mixers add additional calories. Other than energy, alcohol has no nutritional value.

Alcohol Absorption and Metabolism

Ethanol is a small molecule that the body rapidly absorbs through the STOMACH and SMALL INTESTINE and that, once in the BLOOD circulation, readily crosses the BLOOD–BRAIN BARRIER to affect the BRAIN directly. A person generally begins to feel the effects of alcohol within 10 minutes of ingesting an alcoholic drink; the amount of alcohol in the blood circulation peaks about 45 minutes after consumption. Factors that influence the rate of absorption include carbonation and the presence of food. The alcohol from carbonated alcoholic beverages, such as beer and champagne, enters the blood circulation more rapidly than from noncarbonated alcoholic beverages such as wine. Foods, particularly those high in fat and protein, significantly slow the absorption of alcohol.

Once in the blood circulation, however, alcohol metabolizes at a consistent, predictable rate regardless of its ingested form. The body metabolizes alcohol far more slowly than it absorbs alcohol. Though alcohol METABOLISM varies among individuals, in general the body takes 60 to 90 minutes to metabolize one standard drink's worth of the alcohol. Men tend to metabolize alcohol more quickly than women because they have higher quantities of the enzyme acetaldehyde dehydrogenase, which breaks down acetaldehyde (a harmful toxin) to acetic acid (a harmless waste product) that the body can excrete in the URINE.

Ingesting large quantities of ethanol (alcoholic beverages) or of alcohols other than ethanol such as methanol (wood alcohol) and isopropyl alcohol (rubbing alcohol) is potentially fatal.

Alcohol Intoxication

Intoxication (drunkenness) occurs with alcohol consumption because alcohol, which is chemically a solvent, literally softens the neural membranes (the outermost structure of a NEURON), disrupting their ability to respond to electrical impulses (action potential). The highest concentration of neurons is in the brain; the brain neurons most significantly affected appear to be those of the prefrontal cortex, a part of the brain responsible for coordinating numerous functions of cognition, judgment, memory, and inhibition. From a physiologic perspective these changes and the behaviors that result define intoxication. The return to normal follows the same path in reverse, with the less complex functions returning first as the neural membranes essentially "dry out."

Alcohol also alters the presence and balance of chemicals in the brain. Among them are

- gamma-aminobutyric acid (GABA), an inhibitory NEUROTRANSMITTER that carries NERVE impulses in the cerebral cortex to facilitate processes related to inhibitions
- DOPAMINE, a neurotransmitter that is key for nerve impulses related to mood, emotion, and the perception of pleasure
- glutamate, an excitatory neurotransmitter that increases activity among neurons

Alcohol blocks the actions of GABA and glutamate, suppressing the mechanisms in the brain that inhibit inappropriate behaviors and create a

sense of relaxation and calmness. At the same time alcohol increases the presence of dopamine, resulting in feelings of pleasure or even euphoria. With continued, excessive alcohol consumption the brain becomes accustomed to these altered balances and develops reliance on the alcohol to maintain them. At the same time the brain develops TOLERANCE to the presence of alcohol in the blood circulation; it requires higher doses of alcohol to elicit the same neurotransmitter responses.

The physical and mental impairments typically associated with intoxication begins with the most complex skills and progresses to the least complex skills. Because judgment is among the complex skills, by the time a person loses motor function skills (such as balance and coordination) he or she is unable to perceive their deficiencies. Memory storage and retrieval are also high-level skills impaired early in intoxication, accounting for the inability to remember events that happen during intoxication. Long-term, chronic alcohol abuse (frequent, repeated intoxication) alters GENE expression within cells that may result in permanent changes in cell activity.

The uniform standard for legal intoxication in the United States is a blood alcohol concentration (BAC) of 0.08 percent, which represents a measure 80 milligrams of alcohol per deciliter (100 milliliters) of blood. This is the level of alcohol concentration in the blood circulation at which predictable impairments typically occur. However, individuals may appear more or less intoxicated than their BACs suggest because response to alcohol varies.

Health Benefits of Alcohol Consumption

A number of research studies suggest that for most people regular, moderate alcohol consumption—no more than one alcoholic drink daily for women and two alcoholic drinks daily for men—can reduce the risk for CARDIOVASCULAR DISEASE (CVD) such as HYPERTENSION (high BLOOD PRESSURE) and ATHEROSCLEROSIS (fatty deposits in the walls of the arteries). Alcohol affects lipid metabolism, raising levels of high-density lipoprotein (HDL) cholesterol—the "good" cholesterol. It also influences COAGULATION processes, altering the activation of certain coagulation factors in ways that slightly slow blood clotting. Alcohol appears to help relax the smooth MUSCLE of the walls of the arteries, reducing blood pressure. However, health experts caution that people who do not currently drink should not start; the potential health benefits do not sufficiently outweigh the risks. People who should not drink alcohol under any circumstances include those who are in recovery from ALCOHOLISM and pregnant women. People who take prescription drugs should be cautious because alcohol interferes with numerous medications.

Health Risks of Alcohol Consumption

Alcohol toxicity is a serious risk with bouts of heavy or binge drinking in which a person consumes large quantities of alcohol in a short time. A blood alcohol concentration twice the legally defined level of intoxication, 0.16 percent, results in the state of euphoria commonly associated with being intoxicated. At this concentration in the blood circulation alcohol significantly impairs judgment, physical coordination, and reaction time. A blood alcohol level three times the typical legal limit—0.24 percent—causes extreme confusion and possibly stupor. With a blood alcohol level of 0.35 percent the average person is unconscious; 0.50 percent is often a point of no return leading to RESPIRATORY FAILURE and death.

HEALTH RISKS OF ALCOHOL ABUSE

Short Term	
ACCIDENTAL INJURIES	acts of VIOLENCE
alcohol toxicity	impaired cognitive function
impaired judgment	impaired physical coordination
interaction with medications	short-term memory difficulties
reduced inhibition	slurred speech
sleep disturbances	
slowed reaction times	
Long Term	
BERIBERI	CARDIOMYOPATHY
CIRRHOSIS	FETAL ALCOHOL SYNDROME
GASTRITIS	GASTROINTESTINAL BLEEDING
HYPERTENSION	LIVER CANCER
LIVER DISEASE OF ALCOHOLISM	NUTRITIONAL DEFICIENCY
PANCREATIC CANCER	PANCREATITIS
STEATOHEPATITIS	STOMACH CANCER

The primary health consequence of chronic, excessive alcohol consumption is alcoholism. Alcoholism is an addiction to alcohol (physiologic and psychologic dependence on alcohol) and is a

leading health problem in the United States. Secondary to alcoholism is a high risk for LIVER disease. Because it metabolizes alcohol, the liver is the organ most vulnerable to alcohol's toxic effects. Long-term excessive alcohol consumption also increases the risk for LIVER CANCER, STOMACH CANCER, COLORECTAL CANCER, BREAST CANCER, CORONARY ARTERY DISEASE (CAD), hypertension, and NUTRITIONAL DEFICIENCY.

See also ALCOHOLIC HALLUCINOSIS; CELL STRUCTURE AND FUNCTION; DELIRIUM TREMENS; HEPATOTOXINS; ILLICIT DRUG ABUSE; PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

alcohol interactions with medications The numerous ways in which ALCOHOL intensifies or inhibits the actions and side effects of prescription and OVER-THE-COUNTER (OTC) DRUGS. Alcohol also interacts with illicit drugs though often unpredictably because of their uncertain composition. As well, some drugs interact with alcohol in ways that alter alcohol's METABOLISM and actions in the body. Alcohol-medication interactions are of increasing concern as more than 70 percent of Americans take regular medications and at least 10 percent of them drink alcohol daily.

Liver Enzymes and Drug Metabolism

The LIVER produces CYTOCHROME P450 (CYP450) ENZYMES that metabolize (break down into their chemical components) most drugs that enter the body. The enzymes act at predictable rates for specific substances, one of the key factors in establishing appropriate DRUG dosages. Alcohol–medication interactions occur in two general ways: through competition for the enzymes that metabolize them (short-term or acute alcohol consumption) and through changes in the way the liver produces these enzymes (long-term or chronic alcohol consumption). Because the primary interaction between alcohol and medications occurs at this enzyme level, alcohol affects in some way the actions of nearly all medications.

In the short term, acute alcohol consumption (drinking alcoholic beverages) engages the CYP450 enzymes available in the liver. Consequently fewer enzymes are then available to metabolize other substances such as medications. This reduced enzyme access extends the amount and length of time other drugs are active in the BLOOD circulation. The result may be an intensified effect of the drug or an ADVERSE REACTION. For example, drinking while taking antihypertensive medications to treat HYPERTENSION (high BLOOD PRESSURE) may cause blood pressure to drop lower than intended, resulting in dizziness or unsteadiness, especially when standing up after lying down (orthostatic HYPOTENSION).

In the long term, chronic alcohol abuse causes the liver to increase activation of CYP450 enzymes, resulting in more rapid metabolism of drugs. The result may be lower levels of drugs in the blood circulation than are necessary to provide therapeutic effects. With antihypertensive medications, for example, this might mean blood pressure remains elevated beyond the level expected for the DOSE of medication. The alteration of enzyme activity may also metabolize drugs in ways that cause toxicity. Adverse reactions are a particular risk among people who regularly drink alcohol but do not divulge the information to their doctors or often to family members because denial is a hallmark of ALCOHOLISM. Altered enzyme activity may continue for weeks to months after stopping alcohol consumption and may be a permanent state when alcohol abuse has been exceptionally long term (over decades).

Direct Interactions between Alcohol and Other Drugs

Consumed alcohol may also directly compete for or bind with neuroreceptors in the BRAIN in ways that interfere with drugs that act on the CENTRAL NERVOUS SYSTEM such as anesthetic agents, ANALGESIC MEDICATIONS (PAIN relievers), ANTIDEPRESSANT MEDICATIONS, ANTIANXIETY MEDICATIONS, MUSCLE RELAXANT MEDICATIONS, antiseizure medications, ANTIPSYCHOTIC MEDICATIONS, ANTIHISTAMINE MEDICATIONS, and hypnotics. The interaction often intensifies side effects such as sleepiness, confusion, and cognitive dysfunction.

Increased Risk for Liver Damage

As the body's clearinghouse for drugs, the liver is especially vulnerable to damage from toxic byproducts of drug metabolism. Though the liver has great capacity to restore itself, the double

onslaught of hepatotoxic drugs and alcohol may overwhelm its renewal mechanisms. Alcohol is a potent hepatotoxin; it is a poison that destroys liver cells. Many medications are also hepatotoxic and in combination with alcohol consumption can result in significant liver damage and LIVER FAILURE. Some of the most dangerous drugs in combination with alcohol are those in such common use that many people fail to recognize their potential risks or the frequency with which they take them: acetaminophen and the NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS). These drugs are common ingredients in numerous products to relieve symptoms of COLDS, sinus congestion, menstrual cramps, arthritis pain, and general pain (such as in prescription analgesic medications). It is important to minimize or avoid drinking alcohol when taking products that contain these drugs. Various prescription medications are also hepatotoxic themselves or in combination with alcohol.

See also COGNITIVE FUNCTION AND DYSFUNCTION; DRUG INTERACTION; HEPATOTOXINS; ILLICIT DRUG ABUSE; LIVER DISEASE OF ALCOHOLISM; MEDICINAL HERBS AND BOTANICALS; MILK THISTLE; OVERDOSE; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

alcoholic hallucinosis A state of temporary PSYCHOSIS that may occur after sudden withdrawal of ALCOHOL in a person who has heavily consumed alcohol for an extended time. Typical symptoms include auditory and sometimes visual HALLUCINATIONS, PARANOIA, and vivid nightmares. However, thought processes remain clear, and the person remains fully alert and aware of his or her surroundings. Symptoms do not usually require treatment beyond reassurance that they will soon end, though some people benefit from short-term treatment with a BENZODIAZEPINES such as chlordiazepoxide. Most people recover in 10 to 14 days though some symptoms may linger up to 3 weeks.

See also ALCOHOLISM; ANTIANXIETY MEDICATIONS; DELIRIUM TREMENS; SCHIZOPHRENIA; WITHDRAWAL SYNDROME.

alcoholism A health condition resulting from ADDICTION to ALCOHOL. As with other addictions, alcoholism is a combination of physiologic, psychologic, behavioral, and social factors. About 20 million Americans abuse alcohol, at least half of whom have alcohol addiction (alcoholism). Alcoholism has extensive health and social consequences.

Symptoms and Diagnostic Path

A significant factor with alcoholism is hiding the amount of drinking the person is doing. Indications of excessive drinking are often behaviors that might appear normal in isolation but that in aggregate are problematic. These indications may include

- establishing rituals around drinking
- changing plans or missing appointments to drink
- denying drinking or that drinking is a problem
- drinking alone or seeking ways to drink in secret
- hiding bottles of alcohol in odd places
- needing double shots or multiple drinks to feel the effects of the alcohol

Indications of problem drinking that others notice may include

- frequent absences from work or school
- forgetting people, conversations, or events
- unexplained changes in personality or interests
- disappearing at times throughout the day
- out-of-control drinking episodes that the person denies
- frequent illness or health complaints, especially gastrointestinal conditions

The diagnostic path includes physical and psychologic examinations with an initial screening questionnaire about alcohol use. Health-care providers who treat alcoholism use a variety of such screening and assessment tools. Further testing may include diagnostic procedures to diagnose physical health problems associated with alcohol abuse such as LIVER disease, CARDIOVASCULAR DISEASE (CVD), and gastrointestinal disorders. The doctor may also want to test for DIABETES, as chronic alcohol consumption interferes with the GLUCOSE–INSULIN balance. However, there are no BLOOD tests or other procedures to conclusively diagnose alcoholism. The doctor makes the final

diagnosis on the basis of the aggregate findings, including the best determination of the person's drinking patterns and history.

Treatment Options and Outlook

Alcoholism is a chronic, lifelong condition that requires ongoing management to maintain complete abstinence from alcohol. DETOXIFICATION—the process the body goes through to completely eliminate alcohol—takes 5 to 7 days. Medications to ease the symptoms of WITHDRAWAL SYNDROME may include BENZODIAZEPINES and NALTREXONE, which calm anxiety and reduce cravings for alcohol, respectively. After the body is free of alcohol, maintaining sobriety often requires a combination of approaches that may include

- medications such as disulfiram, which prevents the body from metabolizing alcohol, and naltrexone to mitigate alcohol cravings
- individual PSYCHOTHERAPY to gain insight and understanding of the factors that contribute to the desire to drink
- group therapy or SUPPORT GROUPS such as Alcoholics Anonymous to provide opportunity to talk about alcoholism with others who have the condition and to reinforce behaviors to remain drink free

For nearly everyone who has alcoholism, maintaining sobriety (absolute abstinence) requires continued diligence. It is important to seek appropriate intervention to return to sobriety as quickly as possible when relapses do occur. Most alcohol treatment centers and programs also offer support groups and sometimes counseling for family members.

Risk Factors and Preventive Measures

Persistent, regular drinking is the most significant risk for developing alcoholism, because over time the body acquires both alcohol TOLERANCE and alcohol DEPENDENCE. Additive risks include beginning to drink at a young age, family history of alcoholism, genetic composition (separate from family history), and history of psychologic conditions such as ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD), DEPRESSION, and BIPOLAR DISORDER. As well, three in four people who have alcoholism are men.

See also ALCOHOLIC HALLUCINOSIS; DELIRIUM TREMENS; FETAL ALCOHOL SYNDROME; HEPATITIS; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

alkyl nitrites Inhaled drugs that rapidly relax smooth MUSCLE and dilate the BLOOD vessels. The alkyl nitrite with therapeutic application is amyl nitrite, a treatment for ANGINA PECTORIS (CHEST PAIN resulting from constriction of the CORONARY ARTERIES). Amyl nitrite requires a physician's prescription in the United States. Other alkyl nitrites have legitimate uses in products such as room deodorizers, adhesive removers, and various types of cleaners. Medicinal amyl nitrite comes in small glass ampules encased in fabric. To use the vial the person snaps or pops the vial within its protective fabric, releasing and breathing the vapors.

As substances of abuse, alkyl nitrites produce euphoria, reduced inhibition, and a sensation of excitement. Inhaled alkyl nitrites also are reputed to intensify sexual experiences because they relax sphincter muscles such as those in the VAGINA and the ANUS. The primary users of alklyl nitrites are adults between the ages of 30 and 50. Abuse of alkyl nitrites has moderate risk for psychologic DEPENDENCE. OVERDOSE of alkyl nitrites can result in ARRHYTHMIA (irregular heartbeat). Alkyl nitrites may aggravate HYPERTENSION (high BLOOD PRESSURE) or intensify the effects of nitrite-based medications to treat cardiovascular conditions such as hypertension and HEART FAILURE.

COMMON ALKYL NITRITES

amyl nitrite	butyl nitrite
cyclohexyl nitrite	ethyl nitrite
isobutyl nitrite	isopropyl nitrite
methyl nitrite	pentyl nitrite

Long-term use of alkyl nitrites can cause METHEMOGLOBINEMIA, a condition in which the HEMOGLOBIN cannot properly bind with oxygen. Ingestion or injection of alkyl nitrites carries high risk for death. Because alkyl nitrites use tends to encourage high-risk sexual behavior their use results in increased risk for HEPATITIS and SEXUALLY TRANSMITTED DISEASES (STDS) including HIV/AIDS, though alkyl nitrites do not directly cause such infections. Long-term, chronic alkyl nitrites abuse also causes

changes in the function of the IMMUNE SYSTEM that may make users more susceptible to INFECTION.

See also CLUB DRUGS; CORONARY ARTERY DISEASE (CAD); DRUG INTERACTION; SUBSTANCE ABUSE PREVENTION.

amphetamines Drugs that stimulate the CENTRAL NERVOUS SYSTEM. Amphetamines belong to the phenylethylamine class of drugs, a large DRUG family that also includes amphetamine-like drugs with similar actions and effects. Amphetamines and amphetamine-like drugs are SCHEDULED DRUGS in the United States, requiring a physician's prescription for legal use and possession. Those that are schedule 2 drugs further must meet narrowly defined treatment criteria. Methcathinone and cathinone, though ingredients of schedule 2 and schedule 3 drugs, are schedule 1 drugs in their pure forms and do not have therapeutic uses.

Amphetamines and amphetamine-like drugs have dual activity in the BRAIN: They increase the release of serotonin, DOPAMINE, and NOREPINEPHRINE; and they block the reuptake of dopamine, norepinephrine, and monoamine oxidase (MAO). These neurotransmitters have numerous roles in brain activities in regard to mental focus, concentration, and mood. Consequently amphetamines and amphetamine-like drugs increase alertness, reduce APPETITE, and establish a sense of confidence and well-being. Therapeutic uses include treatment for NARCOLEPSY, ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD), weight loss in morbid OBESITY, and alertness in military pilots.

Abuse of amphetamines and amphetamine-like drugs occurs to take advantage of the euphoria, heightened alertness, and diminished need for sleep. As well, the stimulant effects of these drugs may intensify LIBIDO (sex drive), though ERECTILE DYSFUNCTION is a common SIDE EFFECT of chronic abuse. TOLERANCE develops quickly, escalating the amount of drug necessary to produce the desired effects. Because dopamine is also essential for movement, its presence in excess results in involuntary movements (DYSKINESIA). Short-term side effects that usually go away when the drug leaves the body include trembling, HALLUCINATION, increased perspiration, and HEADACHE. Side effects with long-term use that may be long lasting or permanent include SCHIZOPHRENIA-like PSYCHOSIS, PARANOIA, SLEEP DISORDERS, DEPRESSION, ARRHYTHMIA, and aggressive behavior. Amphetamines and amphetamine-like drugs have high risk for psychologic DEPENDENCE and ADDICTION with chronic abuse.

COMMON AMPHETAMINES AND AMPHETAMINE-LIKE DRUGS

amphetamine	benzphetamine
cathinone	dextroamphetamine
diethylpropion	mazindol
METHAMPHETAMIN	Emethcathinone
methylphenidate	phendimetrazine
phentermine	

See also BARBITURATES; CAFFEINE; HYPNOTICS; NARCOTICS; NICOTINE; OPIATES; PERFORMANCE-ENHANCING SUBSTANCES; SUBSTANCE ABUSE TREATMENT.

anabolic steroids and steroid precursors Hormones or hormonelike substances taken to increase MUSCLE mass and STRENGTH. Anabolic steroids are class 3 SCHEDULED DRUGS in the United States, legally available only with a physician's prescription. As substances of abuse, anabolic steroids and steroid precursors (substances the body metabolizes into anabolic steroids) are popular among athletes, bodybuilders, people who work in jobs that require physical strength, and people who desire a particular physique. Anabolic steroids are available in injectable forms and oral tablets.

Therapeutic Uses

Therapeutic uses for anabolic steroids are very limited; many anabolic steroid products are illicit. Though most anabolic steroids are androgenic (increase the production of ANDROGENS, the male sex hormones), anabolic steroids that are nonandrogenic (increase muscle mass without intensifying masculine traits) became available in the late 1990s for therapeutic uses. Anabolic nonandrogenic steroids appear to have fewer undesirable side effects, though the full extent of any long-term consequences remains unknown.

Most commonly doctors prescribe a TESTOSTERONE product for androgen supplementation or therapy and a nonandrogenic anabolic steroid to treat growth-related disorders in children.

Therapeutic uses for anabolic androgenic steroids include treatment for certain kinds of BREAST CANCER and TESTICULAR CANCER, and endocrine disorders in which the body does not produce normal levels of testosterone and other androgens. Therapeutic uses for anabolic nonandrogenic steroids include disorders of the PITUITARY GLAND and other conditions (such as chronic RENAL FAILURE) in childhood that result in smaller than normal stature, and circumstances of muscle loss associated with long-term chronic health conditions such as AIDS.

Abusive Uses

Most anabolic steroid abusers are men ages 20 to 40, though anabolic steroid use among teens (boys and girls) and women, especially athletes, is growing. However, athletic organizations worldwide prohibit the use of anabolic steroids and steroid precursors at all levels of competition from high school through professional. At elite levels of competition, sanctioning organizations use URINE and BLOOD tests to detect anabolic steroid use among competing athletes.

There is some use of anabolic steroids, both androgenic and nonandrogenic, as antiaging therapies. These are unproven uses.

Adverse Health Risks and Consequences

Short-term, adverse health consequences of anabolic androgenic steroids are usually reversible (go away after stopping the DRUG) and may include

- enlarged breasts (GYNECOMASTIA), testicle shrinkage, reduced body HAIR, and other feminization characteristics in men
- facial hair, increased body hair, lowered voice, and other masculinizing characteristics in women
- mood swings, emotional volatility, and outbursts of rage
- moderate to severe DEPRESSION
- DELUSION
- ACNE

Long-term, adverse health consequences of anabolic androgenic steroids are often permanent (continue when no longer taking the drug) and may include

- INFERTILITY or sterility
- LIVER damage
- LIVER CANCER
- left ventricular hypertrophy (enlarged left ventricle of the HEART)
- ATHEROSCLEROSIS and CORONARY ARTERY DISEASE (CAD)

In young people who are still growing, anabolic androgenic steroids cause the growth plates in the long bones to close, ending their growth. Other risks of anabolic steroid use may include INFECTION with HEPATITIS, HIV/AIDS, and other diseases acquired through sharing needles to inject the steroids.

COMMON ANABOLIC STEROIDS AND STEROID PRECURSORS

Anabolic Androgenic Steroids

boldenone	chlorotestosterone
clostebol	dehydrochlormethyltestosterone
dihydrotestosterone	drostanolone
ethylestrenol	fluoxymesterone
formebolone	mesterolone
methandienone	methandienone
methandriol	methandrostenolone
methenolone	methyltestosterone
mibolerone	nandrolone
norethandrolone	oxandrolone
oxymesterone	oxymetholone
stanolone	stanozolol
testolactone	TESTOSTERONE
trenbolone	

Anabolic Androgenic Steroid Precursors

androstenediol	androstenedione
DEHYDROEPIANDROSTERONE (DHEA)	norandrostenediol
norandrostenedione	

Anabolic Nonandrogenic Steroids

human growth hormone (hGH)	insulinlike growth factor 1 (IGF-1)

See also AGING, ENDOCRINE CHANGES THAT OCCUR WITH; ANTIAGING APPROACHES; GAMMA HYDROXYBUTYRATE (GHB); HORMONE; INJECTING DRUGS, RISKS OF; PERFORMANCE-ENHANCING SUBSTANCES.

B

barbiturates DRUGS that depress the functions of the CENTRAL NERVOUS SYSTEM. Barbiturates are SCHEDULED DRUGS in the United States, requiring a physician's prescription for legal use and possession. Some barbiturates are schedule 2 drugs, which strictly limits the reasons for which physicians may prescribe them.

Barbiturates readily cross the BLOOD–BRAIN BARRIER once in the BLOOD circulation and act similarly to ALCOHOL in the ways they affect BRAIN neurons. Though researchers do not know the precise mechanisms through which barbiturates alter brain function, they believe these drugs cause changes in the cell membranes of neurons in a way that alters their action potential (ability to transmit electrical impulses). Researchers do know barbiturates also potentiate (enhance) the presence and activity of gamma aminobutyric acid (GABA), a NEUROTRANSMITTER that regulates many of the brain's inhibitory functions.

Excessive amounts of barbiturates in the blood circulation suppress the respiratory centers in the brain. Barbiturates also slow HEART RATE and lower BLOOD PRESSURE. Combining barbiturates with alcohol is particularly hazardous, as these drugs act in the same ways to depress neurologic function.

Barbiturate OVERDOSE is life threatening and requires emergency medical care. Signs of barbiturate overdose include UNCONSCIOUSNESS, dilated pupils, shallow BREATHING, and slow PULSE.

Barbiturates have numerous therapeutic uses, including sedation during diagnostic and minor surgical procedures, suppression of seizures, and relief of severe anxiety. However, because barbiturates have high potential for ADDICTION and abuse, they are seldom the first line of therapy for most conditions except certain seizure disorders. As drugs of abuse barbiturates are popular for the sense of calm and well-being they can provide and their effectiveness to induce sleep.

COMMON BARBITURATES

amobarbital	aprobarbital
butabarbital	butalbital
mephobarbital	methohexital
pentobarbital	phenobarbital
secobarbital	thiopental

Suddenly stopping barbiturates after long-term use can result in serious or lethal complications, resulting from neurotransmitter imbalance in the

THE TRUTH ABOUT TRUTH SERUM

Thiopental, better known by its trade name Pentothal, is a fast-acting barbiturate that produces a trancelike state of semiconsciousness. One effect of this state is the blockade of inhibition, allowing a person to do and say what the conscious mind might block. Psychiatrists first used sodium pentothal expressly for this purpose when treating what was then called battle fatigue in soldiers returning from World War II. Psychiatrists were able to learn the details of the traumatic experiences the soldiers endured and provide therapy to help them cope with their memories. However, a person under Pentothal's influence does not necessarily answer questions truthfully and indeed may sometimes tell lies once the effect of medication removes the inhibition that would otherwise prevent him or her from doing so.

brain that causes erratic and extreme NERVOUS SYSTEM responses affecting brain function as well as vital functions such as regulation of blood pressure, heart rate, and body temperature.

See also ALCOHOL INTERACTIONS WITH MEDICATIONS; AMPHETAMINES; BENZODIAZEPINES; HYPNOTICS; PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

benzodiazepines Drugs that depress CENTRAL NERVOUS SYSTEM functions. In large part benzodiazepines have replaced BARBITURATES in many therapeutic applications and have numerous therapeutic uses including as MUSCLE relaxants, antianxiety medications, and sleep aids. Doctors also prescribe benzodiazepines to relieve the symptoms of WITHDRAWAL SYNDROME. Benzodiazepines are class 4 SCHEDULED DRUGS in the United States, requiring a physician's prescription for legal use and possession. As drugs of abuse, benzodiazepines are popular for easing the symptoms of "coming down" from other drugs. They may also cause sensations similar to moderate ALCOHOL INTOXICATION. Benzodiazepines are among the most frequently abused prescription medications. Risks of long-term, chronic abuse may result in ADDICTION and symptoms such as HALLUCINATION, trembling, and confusion.

COMMON BENZODIAZEPINES

alprazolam	chlordiazepoxide
clobazam	clonazepam
clorazepate	clorazepate
diazepam	estazolam
flurazepam	halazepam
lorazepam	midazolam
oxazepam	prazepam
quazepam	temazepam
triazolam	

See also GENERALIZED ANXIETY DISORDER (GAD); HYPNOTICS; PRESCRIPTION DRUG ABUSE.

blood doping Actions to boost the ability of the BLOOD to carry oxygen by increasing the volume of red blood cells in the blood circulation. Red blood cells (erythrocytes) contain HEMOGLOBIN, protein molecules that bind with oxygen molecules in the LUNGS. The two commonly used methods of blood doping are BLOOD TRANSFUSION and ERYTHROPOIETIN (EPO) supplementation. Doctors may use either of these methods therapeutically to treat certain types of ANEMIA and to maintain the level of or hasten the return of blood cells after CHEMOTHERAPY. Blood doping is an abuse of these methods done to improve athletic performance by increasing AEROBIC CAPACITY, typically among athletes who compete in ENDURANCE events. However, athletic organizations worldwide prohibit blood doping at all levels of competition, and many routinely test athletes for evidence of it.

Blood Transfusions

Blood transfusion is usually of packed red blood cells and may be homologous (from a donor) or autologous (the person's own blood). For autologous transfusion, the person may undergo HEMOPHORESIS, in which blood withdrawn from the body undergoes cell separation; the components other than the red blood cells are returned to the blood circulation. The concentrated red blood cells collected via hemophoresis are then refrigerated or frozen to store them until a few days before a competition. The athlete receives his or her own red blood cells back via transfusion, boosting the number of red blood cells in the blood. For homologous transfusion, the athlete receives a transfusion of red blood cells collected from donors.

Erythropoietin (EPO)

EPO is a natural HORMONE the body produces to stimulate the BONE MARROW to produce erythrocytes. EPO supplement, which became available in the late 1980s, is a recombinant hormone that intensifies this action. Injections of EPO thus cause the bone marrow to produce extra red blood cells, increasing their presence in the blood. Because it is far easier than blood transfusion to use in secret, EPO is the favored method of blood doping.

Health Risks and Complications

Risks of blood doping include blood clots that can cause HEART ATTACK or STROKE and increased viscosity (thickness) of the blood, which strains the HEART and can cause CARDIOMYOPATHY and HEART FAILURE. Homologous blood transfusions carry the risk of contracting a bloodborne INFECTION such as

HEPATITIS B and hepatitis C, particularly when donation circumvents usual donor screening and collection procedures to minimize detection of the transfusions.

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; ERYTHROCYTE; PERFORMANCE-ENHANCING SUBSTANCES; RECOMBINANT DNA.

buprenorphine A DRUG administered therapeutically to treat opiate ADDICTION. Buprenorphine is available in two formulations: buprenorphine alone for use during DETOXIFICATION; and buprenorphine in combination with NALTREXONE, an opiate antagonist, for long-term use to help prevent recurrence. In the United States buprenorphine is one of the SCHEDULED DRUGS, available only by prescription from a physician who has completed an approved program for its appropriate use in SUBSTANCE ABUSE TREATMENT.

Buprenorphine for opiate addiction treatment is available as sublingual tablets that dissolve under the tongue, releasing buprenorphine for absorption into the BLOOD circulation through the mucosa of the MOUTH. Administered in this way, buprenorphine has an extraordinarily long HALF-LIFE in the body. Because of this, dosing is often every other day in the maintenance phase of treatment. However, it is possible to crush the tablets and mix them with water for injection, which results in a "high" similar to that of HEROIN or other OPIATES. To prevent this, doctors prescribe the buprenorphine with naltrexone formulation (brand name Suboxone in the United States) to help maintain SOBRIETY after initial detoxification when drug cravings may intensify. Very little naltrexone enters the blood circulation through sublingual absorption. However, high amounts enter the blood circulation when dissolved and injected.

Buprenorphine is a synthetic drug that partially binds with opiate receptors, which is enough to activate an opiate response in the body without an intoxication effect. Because of this binding, it is possible to develop a physical DEPENDENCE to buprenorphine. Substance abuse treatment programs taper the dosage over a period of time to wean the body from dependence. Buprenorphine is also available as an analgesic medication (PAIN reliever), which doctors prescribe primarily for pain relief after surgery. Undesired side effects associated with buprenorphine include drowsiness, NAUSEA, CONSTIPATION, and HYPOTENSION (low BLOOD PRESSURE). Buprenorphine OVERDOSE can cause potentially fatal respiratory depression.

See also CYTOCHROME P450 (CYP450) ENZYMES; LEVO-ALPHA ACETYLMETHADOL (LAAM); METHADONE; PRESCRIPTION DRUG ABUSE.

C

caffeine A CENTRAL NERVOUS SYSTEM stimulant. Though not commonly perceived as a DRUG of abuse, caffeine is the most widely used psychoactive drug in the world. The primary sources of caffeine are coffee, tea, and colas. Chocolate also contains some caffeine. A typical cup of coffee contains 100 to 150 milligrams (mg) of caffeine; tea and cola drinks contain 60 to75 mg per serving. Many OVER-THE-COUNTER (OTC) DRUGS, notably those for PAIN relief and relief of menstrual cramps, contain caffeine. Chocolate may contain 3 to 5 mg of caffeine per ounce. Though researchers disagree as to whether caffeine is addictive, many people experience mild withdrawal symptoms when stopping caffeine after long-term consumption of caffeinated beverages. Such symptoms may include HEADACHE, irritability, difficulty concentrating, and cravings for the beverage. Excessive caffeine consumption may cause PALPITATIONS, agitation, and feelings of anxiety.

See also ANALGESIC MEDICATIONS; DYSMENORRHEA; NICOTINE; PERFORMANCE-ENHANCING SUBSTANCES; STIMULANTS.

cannabis The plant *Cannabis sativa*, the source for marijuana, hashish, and hash oil. Cannabis is the most widely used illicit DRUG in the Western world; more than 80 million Americans have used marijuana, the most common form of cannabis, at least once and about 15 million use it regularly. The primary psychoactive chemical in cannabis substances is delta-9-tetrahydrocannabinol, commonly called THC. THC has moderate risk for DEPENDENCE and ADDICTION. ALCOHOL potentiates (enhances and alters) the effects of THC when a person consumes the two drugs together.

Cannabis sativa is among several species of *Cannabis* cultivated in many parts of the world for hemp, the tough fibers of the plant's stem, for use in making rope, floor coverings, nets, and sometimes clothing. Stems and hemp fibers do not contain THC. However, in the United States growth, cultivation, and possession of *Cannabis* are illegal (schedule 1 drug) no matter the reason.

Medical Uses

At present the only accepted medical use of THC is the synthetic formulation dronabinol (Marinol), which doctors may prescribe to treat NAUSEA associated with CHEMOTHERAPY and to improve APPETITE in people who have AIDS. Dronabinol is a schedule 3 drug in the United States; possession and use requires a physician's prescription.

Considerable research has explored the ability of THC to decrease INTRAOCULAR PRESSURE (pressure within the EYE) as a treatment for GLAUCOMA. However, research results have been inconclusive. Though THC (in therapeutic use often referred to as medical marijuana) does lower intraocular pressure the effect lasts only as long as THC is active in the body, about five hours. THC's psychoactive effects make the drug impractical for glaucoma treatment.

Actions and Effects in the Body

THC produces euphoria, heightened or altered sensory perceptions, and a sensation of calm and relaxation. It exerts its psychoactive actions by binding with cannabinoid receptors in the BRAIN. Ordinarily the NEUROTRANSMITTER anandamide binds with these receptors, which are abundant in certain parts of the brain, including the hippocampus, cerebellum, and basal ganglia. The hippocam-

pus regulates memory storage and retrieval for short-term memory. The cerebellum and basal ganglia coordinate and control voluntary motor movement.

THC also binds with neuroreceptors in the brain that affect sensations of pleasure, notably those associated with food and eating. Recent research suggests long-term, chronic use of substances containing THC results in permanent changes to the cannabinoid receptors. Those in the hippocampus seem particularly vulnerable, which researchers believe may account for the long-lasting difficulties chronic marijuana abuses have with short-term memory.

Marijuana

Marijuana is a product formed from the dried leaves and buds of the *Cannabis* plant, which are usually then smoked like cigarettes or in pipes. The psychoactive ingredients, primarily THC, enter the BLOOD circulation rapidly through the LUNGS. The effect lasts about two hours, though THC remains detectable in the blood and URINE for at least 24 hours and up to 10 days after smoking marijuana. Some people mix marijuana with food, in which case THC more slowly enters the blood circulation via absorption through the intestinal mucosa (mucous lining of the SMALL INTESTINE). Most marijuana has a THC content of 5 to 7 percent. A cultivation method that removes the seeds from the plants in their early stages of development results in a particularly potent form of marijuana called sinsemilla, which has a THC content of 10 to 15 percent.

Aside from the neurologic risks of THC, a significant health concern with marijuana is its smoke. Burning marijuana releases more than 400 chemicals, many of which are the same carcinogens (cancer-causing agents) found in cigarette smoke. As well, the smoke is an irritant to the bronchial structures and the lungs. Long-term smoking of marijuana can result in some of the same health problems that result from long-term cigarette smoking such as COUGH, chronic BRONCHITIS and CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). Whether long-term marijuana smoking increases the risk for LUNG CANCER remains unknown, though many researchers believe it has similar carcinogenic characteristics because it contains many of the same chemicals.

Hashish and Hash Oil

Hashish is the dried and compressed resin extracted from the tops of the *Cannabis* plant. As with marijuana, the most common methods of consumption are smoking (though typically in pipes) and cooking in foods. Its THC content is 5 to 7 percent. Hash oil is an extract of the THC and other cannabinoids (cannabis chemicals) pulled from the flowers of *Cannabis* plants using a solvent. The resulting liquid is thick and concentrated, with a THC content of about 15 percent. The user may place a few drops on an ordinary cigarette or in foods. The effects and their duration for both hashish and hash oil are similar to marijuana.

HEALTH RISKS OF CANNABIS ABUSE

Short Term	
altered judgment and relaxed inhibition	anxiety
delayed reaction time	cognitive dysfunction
heightened sensory perceptions	dizziness
increased APPETITE	impaired balance and coordination
panic attack	
Long Term	
apathy and disinterest in life	delusions
DEPRESSION	IMMUNE SYSTEM suppression
loss of short-term memory functions	PSYCHOSIS

See also COGNITIVE FUNCTION AND DYSFUNCTION; ILLICIT DRUG USE; MEMORY AND MEMORY IMPAIRMENT; SCHEDULED DRUGS; SUBSTANCE ABUSE TREATMENT.

chloral hydrate A hypnotic drug used therapeutically as a sleep aid. Chloral hydrate is a schedule 4 drug in the United States, requiring a physician's prescription for legal use and possession. As a drug of abuse chloral hydrate may be taken alone or mixed with ALCOHOL ("Mickey Finn"). The latter produces a potent sedative as well as amnesiac effect. Such a mixture gained notoriety as a "date rape" concoction in the early decades of the 20th century. When taken at therapeutic dosage chloral hydrate is very safe. However, at high doses, chlo-

ral hydrate may produce potentially fatal respiratory depression.

HEALTH RISKS OF CHLORAL HYDRATE ABUSE

Short Term	
ARRHYTHMIA	disturbed balance and coordination
dizziness	impaired motor function
HALLUCINATION	slurred speech
irritability	
Long Term	
HEART damage	kidney damage
LIVER damage	sleep disturbances

See also FLUNITRAZEPAM; GAMMA HYDROXYBUTYRATE (GHB); HEPATOTOXINS; HYPNOTICS; SCHEDULED DRUGS; SEXUAL ASSAULT.

club drugs Drugs popular for illicit use in settings such as "rave" clubs and at parties. Most club drugs are designer drugs though some are conventional drugs used illicitly. The key risks with club drugs are not knowing what they are when taking them and combining them with ALCOHOL.

Among the most popular club drugs are HALLUCINOGENS such as KETAMINE and METHYLENEDIOXYMETHAMPHETAMINE (MDMA), commonly called ecstasy, and HYPNOTICS such as FLUNITRAZEPAM (Rohypnol), commonly called rophies or roofies, and GAMMA HYDROXYBUTYRATE (GHB). Flunitrazepam and GHB, which are odorless and tasteless, have gained notoriety as "date rape" drugs because they produce amnesia of events that occur during the time of the drug's effectiveness in the body. Other drugs sometimes popular as club drugs include LSD and METHAMPHETAMINE.

Mixing any of these drugs with alcohol is particularly hazardous and can result in potentially fatal respiratory depression.

See also DESIGNER DRUG; MEMORY FUNCTION AND IMPAIRMENT; SCHEDULED DRUGS.

cocaine A DRUG that acts as a CENTRAL NERVOUS SYSTEM stimulant. Cocaine is highly addictive and is a schedule 2 drug in the United States, subjecting its legal use to stringent requirements. The primary therapeutic use of cocaine is as a topical anesthetic applied to the mucous membranes for dental and surgical operations. Cocaine is a popular drug of abuse, and an estimated 35 million Americans have used it at least once.

Extracted from the leaves of the *Erythroxylum coca* plant, cocaine as a drug of abuse produces intense euphoria, energy, and a sense of physical and mental infallibility. The most common method of use is to snort (rapidly inhale) the powdered form of the drug into the NOSE, where absorption through the nasal mucosa (mucous membrane lining of the nose) allows the drug to enter the BLOOD circulation within a few minutes for an effect that lasts two to three hours. Crack cocaine—created by mixing cocaine powder with sodium bicarbonate and water, then igniting the dried mixture and inhaling the smoke—gets the drug into the blood circulation even more rapidly through the LUNGS. Some people dissolve the powder in water and inject the solution intravenously for an instant and intense though short (20 to 30 minutes) effect.

The key risk of cocaine abuse is ADDICTION; about 10 percent of people who try cocaine eventually become addicted. Crack cocaine is particularly addictive. The compulsion to use cocaine is so intense for many people who are addicted that they resort to extraordinary actions to acquire the drug. The person trying to quit cocaine often needs short-term medical support to mitigate symptoms of withdrawal and long-term family and social support to stay off cocaine.

HEALTH RISKS OF COCAINE ABUSE

Short Term	
anxiety	diminished ability to feel PAIN
elevated body temperature	HEART ATTACK
HYPERTENSION	PARANOIA
rapid HEART RATE	restlessness, irritability, or agitation
Long Term	
ADDICTION	ARRHYTHMIA
chronic nasal congestion	DYSPNEA (difficulty BREATHING)
HALLUCINATION	MALNUTRITION
PSYCHOSIS	runny NOSE (RHINORRHEA)
seizures	SUDDEN CARDIAC DEATH

Though the effects on fetal development when a pregnant woman uses cocaine are uncertain the infant can be born with cocaine addiction, especially if the mother is using crack cocaine. Because many women who abuse cocaine also drink ALCO-

HOL and smoke cigarettes, both of which affect fetal development, health consequences for infants born to cocaine-addicted mothers are often multiple and complex. Infants born addicted to cocaine require extensive medical care until their bodies are free from the effects of the drug. They are also more likely to be born prematurely, increasing the need for medical care during early infancy as well as the risk for lifelong health problems, including developmental delays and LEARNING DISORDERS later in life.

Cocaine abuse may also cause changes in cardiovascular function that can result in sudden HEART ATTACK in users of any age and during any use of the drug, including the first time. Researchers do not know what causes such cardiovascular changes or their precise nature, though speculate the cardiovascular effect is a combination of conductive (ARRHYTHMIA) and ischemic (severely decreased blood flow and oxygen supply to the HEART MUSCLE) circumstances that collude to cause the heart to suddenly stop beating.

See also AMPHETAMINES; ANESTHESIA; ILLICIT DRUG USE; SCHEDULED DRUGS; STIMULANTS; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

D

delirium tremens A serious medical condition that may develop during withdrawal from ALCOHOL ADDICTION (ALCOHOLISM). The symptoms of delirium tremens are both physical and psychologic; the physical symptoms can be life threatening without prompt medical treatment. Most people who experience delirium tremens (also called DTs) are long-term heavy drinkers who suddenly quit drinking. However, delirium tremens may also occur after a single episode of extreme alcohol consumption in a person who does not often drink heavily.

Delirium tremens develops as a consequence of the BRAIN's inability to restore the balance among the neurotransmitters gamma-aminobutyric acid (GABA), DOPAMINE, and glutamate. Instead the imbalance that resulted from alcohol DEPENDENCE spirals out of control, producing a spectrum of autonomic dysfunctions that affect multiple body systems.

Symptoms begin within a few to 48 hours of alcohol cessation and are often severe from the onset. Symptoms may include

- tremors and seizures
- hyperactive reflexes
- confusion, DELUSION, and HALLUCINATION
- anxiety, irritability, restlessness, and agitation
- tachycardia (rapid HEART RATE), TACHYPNEA (rapid BREATHING), diaphoresis (excessive sweating), and PALPITATIONS
- elevated body temperature and BLOOD PRESSURE
- NAUSEA and VOMITING

Diagnostic tests may include BLOOD tests to measure blood alcohol concentration, LIVER enzyme levels, and complete blood count (CBC). The doctor may desire other tests to evaluate specific symptoms, such as ELECTROCARDIOGRAM (ECG) for palpitations and tachycardia. Treatment is generally intravenous administration of BENZODIAZEPINES, such as chlordiazepoxide and diazepam, to produce sedation and to help stabilize the NEUROTRANSMITTER balance in the brain because benzodiazepines also bind with GABA neuroreceptors. Without treatment delirium tremens may so significantly disrupt brain function as to cause death. With appropriate and timely treatment, symptoms end in about 72 hours and most people recover completely in 7 to 10 days.

See also ALCOHOL HALLUCINOSIS; NALTREXONE; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

dependence The physiologic or psychologic need to continue taking a particular DRUG. In physiologic dependence, predictable changes occur within the body that reconfigure or adapt a particular facet of function and result in the body's reliance on the substance to maintain that function. Often the body then reacts in unpleasant ways (WITHDRAWAL SYNDROME) when the person stops taking the substance. Physiologic dependence ends when the body completely clears all chemical traces of the drug. Drugs often subject to abuse that cause physiologic dependence include ALCOHOL, HEROIN, and opiate NARCOTICS such as morphine, hydrocodone, and oxycodone.

In psychologic dependence taking the drug results in pleasurable sensations and the desire (craving, when intense) to take the substance to obtain them. Though the drug causes chemical changes in the body that result in temporary alterations of function, the drug does not establish any physiologic adaptation. Psychologic dependence can be intense and does not correlate to the drug's

presence in the body. Because the body develops TOLERANCE to many drugs taken on a long-term basis (requiring a higher DOSE to achieve the same effect), the longer the person uses the substance the more likely he or she may experience some physiologic and psychologic symptoms when stopping the substance, representing the body's adaptation to the drug's absence. The nature of such symptoms depends on the drug. Drugs often subject to abuse that cause psychologic dependence include COCAINE, AMPHETAMINES, BENZODIAZEPINE drugs, and HALLUCINOGENS.

Though drug dependence is often a key factor in substance abuse and ADDICTION, it is not synonymous with either. Substance abuse and addiction encompass the ways in which people use the drugs and the behaviors in which they engage to obtain the drugs. Physiologic dependence occurs in numerous therapeutic applications—for example, with therapies involving systemic CORTICOSTEROID MEDICATIONS, ANTIDEPRESSANT MEDICATIONS, and antihypertensive medications. As well, a person may develop dependence on a substance commonly abused (such as a narcotic PAIN reliever or antianxiety medication) when taking it to legitimately treat a health condition and yet not abuse or have an addiction to that substance.

Symptoms and Diagnostic Path

Indications of drug dependence vary according to the drug. In a therapeutic context such symptoms reflect achievement of the desired effect of the drug—for example, suppression of the IMMUNE RESPONSE with corticosteroid medications or relief of symptoms with antidepressant medications or pain relief medications. In the context of substance abuse or addiction, indications of drug dependence may include attempts to obtain increasing quantities of the drug, taking the drug inappropriately, and obvious differences in behavior between when taking the drug and when not taking the drug.

Treatment Options and Outlook

Treatment for undesired or unintentional drug dependence, such as with corticosteroid or antidepressant medications, consists of controlled weaning from the drug, a process that may take several weeks to complete. In circumstances in which there is also substance abuse or addiction, extensive support and treatment such as PSYCHOTHERAPY are also essential. Though physiologic dependence ends when the drug is no longer present in the body, psychologic dependence can persist for weeks, months, or even years after stopping the drug.

Risk Factors and Preventive Measures

The primary risk factor for drug dependence is taking repeated doses of the drug. When doing so is to achieve therapeutic outcomes, drug dependence is desired and appropriate. When the purpose of taking a drug is other than therapeutic, not only is dependence possible but there is a high likelihood for substance abuse or addiction. As such use is detrimental to health, prevention efforts include restricting access to the drug along with education and therapy, if appropriate, to understand the health consequences of continued dependence and behavioral approaches to avoid use of the drug.

See also ANALGESIC MEDICATIONS; ILLICIT DRUG USE; PRESCRIPTION DRUG ABUSE; SCHEDULED DRUGS; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

depressants Chemicals that slow the activity of the CENTRAL NERVOUS SYSTEM. The primary therapeutic purpose of depressants is to cause sedation or sleep. Most work through actions that directly affect the function of BRAIN neurons, neurotransmitters, and neuroreceptors. Many do so by increasing the activity of gamma aminobutyric acid (GABA), a NEUROTRANSMITTER that slows brain function. Depressants have high potential for DEPENDENCE and ADDICTION. Abruptly ending their use may cause WITHDRAWAL SYNDROME that, with certain drugs, has the potential to be life threatening when symptoms are serious and untreated.

Types of prescription drugs that are depressants include ANTIANXIETY MEDICATIONS, HYPNOTICS, BARBITURATES, and BENZODIAZEPINES. Drugs in these classifications are SCHEDULED DRUGS in the United States, which require a physician's prescription for legal possession and use. Doctors may prescribe them to treat GENERALIZED ANXIETY DISORDER (GAD), panic attacks and PANIC DISORDER, SLEEP DISORDERS, and POST-TRAUMATIC STRESS DISORDER (PTSD).

As substances of abuse, depressants produce INTOXICATION with initial euphoria and subsequent diminished cognitive function. Those who abuse depressants often do so to dull the effects of coming down from other drugs such as METHAMPHETAMINE and COCAINE. The most commonly abused depressants are ALCOHOL and benzodiazepines, notably alprazolam and diazepam. Other commonly abused depressants include the illicit drugs FLUNITRAZEPAM and GAMMA HYDROXYBUTYRIC ACID (GHB).

See also ALCOHOLISM; ILLICIT DRUG USE; PRESCRIPTION DRUG ABUSE; STIMULANTS.

designer drugs Illicit drugs created by altering the molecular structure of existing drugs, usually drugs that are legal but restricted. The designer drug is typically similar to the derivative drug in its actions and effects, though both are often enhanced or intensified in some way. Because "street chemists" (commonly called cookers) manufacture designer drugs in casual settings, these drugs are often of inconsistent potency and purity. There are often dozens of variations on a particular formula, each somewhat different molecularly but all touted as the same drug.

Most designer drugs are CLUB DRUGS produced solely for the purpose of creating an intoxicating or hallucinogenic experience, though some designer drugs are substances people take to improve physical or athletic performance. The risk for OVERDOSE, either from a single unexpectedly potent dose or through combining drugs, is very high. Designer drugs have no therapeutic use.

See also AMPHETAMINES; BLOOD DOPING; HALLUCINOGEN; METHAMPHETAMINE; PERFORMANCE-ENHANCING SUBSTANCES; SUBSTANCE ABUSE PREVENTION.

detoxification The process of eliminating from the body a substance to which a person is addicted. Detoxification causes physiologic changes that restore to normal the way the body functions, reversing the changes that occurred as DEPENDENCE and ADDICTION developed. This process of restoration can cause symptoms such as ABDOMINAL PAIN, JOINT and MUSCLE PAIN, NAUSEA, VOMITING, "shakes" (tremors), and sometimes seizures.

Controlled detoxification, also called medically supervised withdrawal, is the first stage of treatment for DRUG addiction (including ALCOHOL addiction). Many people undergoing treatment for addiction receive medications to mitigate withdrawal symptoms. Detoxification may take as long as 14 days, though the most severe symptoms occur within the first 3 to 5 days for most addictions. Successful recovery from addiction requires further, and often ongoing, treatment that may include PSYCHOTHERAPY, BEHAVIOR MODIFICATION THERAPY, COGNITIVE THERAPY, and intensive family and peer support.

See also ALCOHOLIC HALLUCINOSIS; ALCOHOLISM; INTOXICATION; SOBRIETY; WITHDRAWAL SYNDROME.

dextromethorphan A COUGH suppressant, also called an antitussive, that is a common ingredient in numerous OVER-THE-COUNTER (OTC) DRUGS. These products are the most common sources for abuse, though other sources include illicit dextromethorphan powder or capsules that contain dextromethorphan powder. Though not a narcotic, dextromethorphan binds with certain opiate receptors in the BRAIN and SPINAL CORD (CENTRAL NERVOUS SYSTEM) and has an opioid effect in suppressing the cough REFLEX. Dextromethorphan has low risk for DEPENDENCE or ADDICTION.

At the recommended DOSAGE in cough and cold relief products dextromethorphan effectively relieves cough without significant side effects. When taken in amounts that exceed the recommended dosage dextromethorphan causes NAUSEA, disorientation, HALLUCINATION, and dissociation (perceptions of separating from the physical body). In very high doses, dextromethorphan causes confusion, slurred speech, disturbed vision, tachycardia (rapid HEART RATE), and peripheral PARESTHESIA (tingling and numbness of the fingers and toes). Seizures or fatal ARRHYTHMIA (irregular HEART beat) may also occur with very high doses. Chronic dextromethorphan abuse may result in PSYCHOSIS and permanent neurologic damage to the brain.

Other ingredients in multisymptom products that contain dextromethorphan, such as acetaminophen (an analgesic and antipyretic) and guaifenesin (an expectorant), may cause other undesired side effects. Chronic acetaminophen use or acetaminophen OVERDOSE has high risk for permanent LIVER damage, LIVER FAILURE, kidney damage, and RENAL FAILURE.

HEALTH RISKS OF DEXTROMETHORPHAN ABUSE

Short Term	
confusion	disorientation
double vision	HALLUCINATION
NAUSEA and VOMITING	seizures
sudden death	tachycardia (rapid HEART beat)

Long Term	
ARRHYTHMIA	BRAIN damage
chronic hallucinations	neuromotor dysfunction

See also ANALGESIC MEDICATIONS; HALLUCINOGENS; HEPATOTOXINS; NARCOTICS; OPIATES; PRESCRIPTION DRUG ABUSE.

disulfiram A medication that blocks the action of the enzyme acetaldehyde dehydrogenase in the second stage of ALCOHOL METABOLISM. This inhibition prevents the conversion of acetaldehyde, a potent toxin, to relatively harmless acetic acid. The consequence is rapid accumulation of acetaldehyde in the BLOOD circulation, causing an array of extremely unpleasant symptoms similar to severe hangover. The intensity of symptoms correlates directly to the DOSE of disulfiram and the amount of alcohol consumed.

Disulfiram, better known by its trade name Antabuse, may be among the treatments for ALCOHOLISM. Though disulfiram is very effective for controlling alcohol consumption, it does not cure alcoholism. Symptoms that occur with the combination of disulfiram and alcohol, called the disulfiram–alcohol reaction, include

- throbbing HEADACHE
- intense thirst and profuse VOMITING
- excessive sweating
- PALPITATIONS and CHEST PAIN
- blurred vision
- HYPERVENTILATION and DYSPNEA (shortness of breath)

Symptoms typically begin about 10 minutes after consuming alcohol and last 60 to 90 minutes. Though disulfiram can be very effective in helping maintain SOBRIETY in people who stringently comply with the conditions of treatment, it can cause severe and potentially life threatening symptoms when alcohol consumption is substantial. Such severe symptoms require emergency medical attention. Among them are tachycardia (rapid HEART RATE), ARRHYTHMIA (irregular HEART rate), seizures, and RESPIRATORY FAILURE.

Because so many products and substances, including medications, can contain ALCOHOL, health-care providers recommend that anyone taking disulfiram carry a wallet card that identifies them as on disulfiram therapy and the contact information for the prescribing physician.

Abstinence from alcohol prevents symptoms. It is essential to avoid all products that contain alcohol. Common sources of alcohol include alcoholic beverages (beer, wine, mixed drinks), salad dressings, food sauces, cough and cold preparations, any medicinal preparations labeled elixirs, mouthwashes, and some COLD SORE treatments. Topical products that contain alcohol, such as aftershave lotion, may also activate the disulfiram–alcohol reaction. Ingesting alcohol in any quantity in the 12 hours before the first disulfiram dose or up to 14 days after the last disulfiram dose will produce symptoms.

See also INTOXICATION; METHADONE; NALTREXONE.

E–G

ecstasy See METHYLENEDIOXYMETHAMPHETAMINE (MDMA).

ethchlorvynol A sedating hypnotic DRUG, similar in physiologic action and effects to BARBITURATES, doctors may prescribe as a sleep aid to treat insomnia. Ethchlorvynol (brand name Placidyl) has high potential for physical DEPENDENCE and ADDICTION, however, and is seldom the medication of first choice in a therapeutic setting. It is a schedule 4 drug in the United States; possession and use are legal only with a doctor's prescription.

TOLERANCE to ethchlorvynol develops after about one week of taking it regularly, which means the body requires a higher DOSE to achieve the same effect. Taking ethchlorvynol for three weeks or longer often establishes physical dependence; abruptly stopping the drug after this time is likely to result in withdrawal symptoms such as NAUSEA, agitation, HALLUCINATION, tremors ("shakes"), and possibly seizures. It is important to taper the amount of drug over days to weeks to stop taking it. As a drug of abuse, ethchlorvynol produces an intoxicating effect. As with other hypnotics, combining the drug with ALCOHOL enhances the sedating effect and can result in OVERDOSE. People who abuse substances such as METHAMPHETAMINE or COCAINE may use ethchlorvynol to ease the transition between the "high" of the stimulant and the "crash" of returning to normal state.

See also CHLORAL HYDRATE; DEPRESSANTS; HYPNOTICS; PRESCRIPTION DRUG ABUSE; SCHEDULED DRUGS; STIMULANTS; WITHDRAWAL SYNDROME.

fentanyl A narcotic PAIN reliever about 80 times more potent than morphine. Fentanyl's primary therapeutic uses are for intravenous anesthetic during surgery and for analgesia (pain relief) after major operations such as OPEN HEART SURGERY or to treat significant CHRONIC PAIN such as may occur with terminal cancer. Fentanyl is a schedule 2 DRUG in the United States, strictly regulating its legitimate use. Numerous analogs (pharmacologic derivations) of fentanyl are available illicitly, though only a few are available for legitimate use.

As a drug of abuse fentanyl produces effects similar to those of HEROIN though is significantly more potent. The most common method of administration, as with heroin, is intravenous injection (using a needle to inject the drug directly into a VEIN). Other forms of fentanyl subject to abuse are transdermal patches (Duragesic) and a "lollipop" that allows the drug to enter the BLOOD circulation by being absorbed through the mucous membrane of the MOUTH (transmucosal absorption). The risk for OVERDOSE is very high with abuse of these forms of fentanyl, as their structure releases a consistent amount of the drug over an extended period of time and consuming them faster than intended releases excessive amounts of the drug. Fentanyl has a high risk for DEPENDENCE and ADDICTION, with significant withdrawal symptoms when stopping the drug.

See also ANALGESIC MEDICATIONS; ANESTHESIA; ILLICIT DRUG USE; KETAMINE; OPIATES; PHENCYCLIDINE (PCP); PRESCRIPTION DRUG ABUSE; SCHEDULED DRUGS; WITHDRAWAL SYNDROME.

fetal alcohol syndrome A constellation of BIRTH DEFECTS that may occur as a result of a woman's ALCOHOL consumption during the early stages of PREGNANCY. About 6,000 infants are born with fetal alcohol syndrome (FAS) each year in the United States. Up to five times as many more infants are born with symptoms of alcohol exposure during prenatal development, although they do not have

full-blown FAS. Doctors may call incomplete forms of FAS alcohol-related neurodevelopmental disorder (ARND) when symptoms are primarily behavioral and alcohol-related birth defects (ARBD) when symptoms are primarily physical. People sometimes refer to the entire range of these conditions as fetal alcohol spectrum disorders (FASDs), though this is a general rather than a clinical term.

Researchers first identified FAS in 1981 and are still unable to determine any safe level of drinking during pregnancy. Alcohol is highly teratogenic, meaning it has strong capability to cause damage to cells of all types during fetal development. The highest risk for severe birth defects occurs with heavy drinking during the first eight weeks of pregnancy, the time when body systems and organs are developing. The BRAIN and NERVOUS SYSTEM are particularly vulnerable to alcohol toxicity; exposure during any stage of pregnancy may affect whatever neurologic development is occurring at the time. The result may be a range of intellectual, emotional, and behavioral dysfunctions that become apparent as the child grows up.

Symptoms and Diagnostic Path

A collaboration of US health-care agencies convened as the National Task Force on Fetal Alcohol Syndrome and Fetal Alcohol Effects issued diagnostic criteria and guidelines in 2004, under mandate from the US Congress to establish consistent diagnosis. These criteria include

- small head (microcephaly) with structural brain abnormalities apparent with diagnostic imaging procedures
- three unique and characteristic craniofacial anomalies, also called facial dysmorphias: smooth philtrum (no ridges in the upper lip); narrowly placed eyes with short slits (palpebral fissures); and narrow, thin upper lip
- impaired growth (height or weight that remains below the tenth percentile for age)
- mental delays and functional deficits (varied and numerous intellectual, cognitive, and behavioral problems)

Some infants who have FAS also have other birth defects. Prenatal exposure to alcohol may be the affirming factor, though the collective characteristics of FAS are relatively unique to the effects of alcohol. Mild symptoms are sometimes difficult to detect and diagnose, especially when health-care providers do not know the mother's alcohol consumption during pregnancy (as is common in many adoption circumstances). From initial establishment of FAS criteria, the diagnostic path includes further neurologic and psychologic testing to more concisely define the extent of the damage.

Treatment Options and Outlook

Treatment attempts to manage symptoms and the effects of the damage that has occurred. The earlier diagnosis takes place and interventions can begin, the more successful treatment usually is in helping the child reach his or her full potential. Children who have FAS are more likely also to have psychologic conditions such as ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) and CONDUCT DISORDER. The first children diagnosed as having FAS are only now entering adulthood, so doctors do not know the long-term consequences of FAS. People who have mild symptoms and receive aggressive, targeted intervention are often able to function in society with relative success. Those who have severe symptoms may need ongoing care even in adulthood.

Risk Factors and Preventive Measures

The only risk for fetal alcohol syndrome is a woman's consumption of alcohol during pregnancy. FAS is entirely preventable if the woman completely abstains from alcohol during pregnancy, from CONCEPTION to birth. Because more than half of pregnancies in the United States are unplanned, the greatest risk exists for women who are not planning pregnancy but become pregnant.

Extensive education efforts have increased awareness of the dangers of alcohol during pregnancy, among them warning labels placed on alcoholic beverage containers and posted in establishments that serve alcoholic beverages such as restaurants, lounges, taverns, and bars. However, many people, including some health-care providers, still erroneously believe it is safe to drink in moderation during pregnancy. The US

Surgeon General in 2005 issued an advisory stating that there is no safe threshold for alcohol consumption during pregnancy and that the risk for FAS and related conditions increases with the amount and frequency of alcohol a woman consumes during pregnancy.

See also ALCOHOLISM; PRENATAL CARE; SUBSTANCE ABUSE TREATMENT.

flunitrazepam A hypnotic DRUG with sedative actions and effects similar to those of other BENZODIAZEPINES. Flunitrazepam, better known by its brand name Rohypnol or its slang names ropies and roofies, is not legal in the United States, though it is manufactured as a legal drug in other countries. As a drug of abuse flunitrazepam is popular at parties and in clubs. Taken alone it produces a euphoric INTOXICATION. When combined with ALCOHOL flunitrazepam causes incapacitation and amnesia of events that take place while the drug combination is active in the body. Because of this interaction flunitrazepam has gained notoriety as a "date rape" drug. The risks for DEPENDENCE and ADDICTION are moderate.

See also CLUB DRUGS; DEPRESSANTS; DETOXIFICATION; SCHEDULED DRUGS; WITHDRAWAL SYNDROME.

gamma hydroxybutyrate (GHB) An illicit DRUG with depressant and anabolic effects in the body, depending on the amount and frequency taken. GHB originally gained popularity among bodybuilders and athletes for whom STRENGTH and MUSCLE mass are important. Though not a HORMONE, GHB has anabolic effects—that is, it causes an increase in both the number and size of voluntary muscle cells. Its sedative qualities also make GHB an effective sleep aid for people also using other anabolic steroids, which tend to cause sleep disturbances.

As a CENTRAL NERVOUS SYSTEM depressant, GHB functions as a hypnotic with moderate sedating action. Combining GHB with ALCOHOL greatly intensifies this action, resulting in rapid and deep sleep with amnesia; the person does not remember events that occur during the INTOXICATION period. As a consequence GHB has acquired notoriety as a "date rape" drug, used to unknowingly intoxicate others for the purpose of SEXUAL ASSAULT.

GHB is a schedule 1 drug in the United States, indicating that it has no known therapeutic use. A legal, uncontrolled GHB precursor to is 1,4-butanediol, a chemical commonly available as an industrial solvent. 1,4-butanediol metabolizes to GHB after ingestion and has the same effects in the body. Efforts are under way in the United States to reclassify 1,4-butanediol to restrict its availability as well.

See also ANABOLIC STEROIDS AND STEROID PRECURSORS; CLUB DRUGS; DEPRESSANTS; HYPNOTICS.

glutethimide A hypnotic DRUG first used as a substitute for BARBITURATES to treat insomnia and other SLEEP DISORDERS. Glutethimide (brand name Doriden) is highly addictive, and, like barbiturates, poses a significant risk for life-threatening symptoms when taken in excessive amounts. TOLERANCE to the drug (increased amount necessary to produce the same effect) occurs after about a week of regular use; DEPENDENCE may develop after three weeks of regular use. Stopping the drug suddenly after three weeks or longer of regular use often results in withdrawal symptoms that may require medical treatment. Because of its high risk for ADDICTION and OVERDOSE, glutethimide is a schedule 2 drug in the United States and requires a physician's prescription for legal possession and use. Few physicians prescribe glutethimide, however, because other sedatives and hypnotics are as effective with fewer side effects and lower risk for addiction.

See also HYPNOTICS; PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

hallucinogens Psychoactive substances that alter the BRAIN's perceptions of sensory experiences. Auditory and visual HALLUCINATION, time disorientation, and altered depth perception are common with hallucinogen abuse. However, not all people who take hallucinogens experience hallucinations. Researchers do not know the precise mechanisms of hallucinogens though believe many of them affect the presence of serotonin, a NEUROTRANSMITTER in the brain. Most hallucinogens are illicit substances; many come from natural sources such as mushrooms and cacti and others are synthesized (created in clandestine laboratories using chemicals). In the United States hallucinogens are SCHEDULED DRUGS; most are schedule 1 drugs because there are no therapeutic applications for their use and they have such high abuse potential.

Short-term, adverse health consequences of hallucinogen use include distortions of reality that may lead to irrational decisions and actions. Rapid mood swings and corresponding changes in behavior are common. The effective action of some hallucinogens may be 10 hours or longer. Long-term, adverse health consequences of chronic hallucinogen use include possible neurotoxicity and death of brain neurons. Some people experience flashbacks—hallucinatory experiences that repeat days, weeks, and sometimes months after hallucinogen use. Occasionally PSYCHOSIS develops in a person who uses hallucinogens extensively. Hallucinogen use does not typically result in DEPENDENCE though may result in ADDICTION (desire to take the DRUG).

Lysergic Acid Diethylamide (LSD)

The original purpose of lysergic acid diethylamide (LSD), first synthesized in 1938, was as a treatment to prevent seizures. However, testing did not bear out this potential. Through incidental ingestion, LSD's developer, Swiss chemist Albert Hofmann (b. 1906), discovered the drug's hallucinogenic capabilities. Because the effects of taking LSD could be remarkably similar to the some types of SCHIZOPHRENIA, researchers subsequently used LSD in clinical research as an effort to better understand this psychiatric disorder. However, LSD proved unable to provide the insights researchers hoped it would. In the 1960s LSD became popular as an illicit hallucinogen.

LSD is a very potent hallucinogen that can remain active in the body up to 12 hours. High doses often generate unpleasant or frightening experiences and tend to produce flashbacks for two to three days after its use. Common initial effects include rapid HEART RATE, NAUSEA, low body temperature, and diaphoresis (cold sweat). Hallucinations begin about an hour after ingestion and may result in bizarre behavior as the person reacts to distorted sensory perceptions. Some people experience intense anxiety and DEPRESSION after the effect of the LSD wears off.

Natural Hallucinogens

Natural sources of hallucinogenic substances are abundant and include plants such as cacti, which contain mescaline, and numerous types of mushrooms, which contain tryptamines such as psilocybin. Some natural hallucinogenic substances are potentially lethal even in small doses. Tryptamine-containing mushrooms grow abundantly in hot, moist environments around the world, including in the United States. The peyote cactus (*Lophophora williamsii*) grows abundantly in the southwestern United States and northern Mexico. The peyote's crowns contain high concentrations of mescaline. The most common methods of

ingestion are chewing or eating dried plants or mushrooms or drinking liquid brewed from them. The potency and effect of natural hallucinogens are unpredictable.

Other Drugs with Hallucinogenic Effects

Many substances can generate hallucinatory experiences, particularly when taken in high doses. Hallucinations, especially visual, are common with abuse of many types of AMPHETAMINES and NARCOTICS. Among such drugs are

- METHYLENEDIOXYMETHAMPHETAMINE (MDMA), better known by its slang name ecstasy, a popular amphetamine-based club drug that produces a combination of euphoria and excitation
- KETAMINE, an anesthetic agent seldom used for ANESTHESIA in people because it produces hallucinations and sometimes DELIRIUM
- PHENCYCLIDINE (PCP), a veterinary anesthetic agent that produces intense hallucinations, DELUSION, delirium, and other psychoactive responses in people

These drugs also produce primary effects such as CENTRAL NERVOUS SYSTEM stimulation, analgesia (PAIN relief), and anesthesia (unawareness of sensation). When used as drugs of abuse, the overall effects are often unpredictable. Illicit chemists often mix different drugs together to create variations of these drugs, which are particularly harmful because their actions are unknown in such combinations.

COMMON HALLUCINOGENS

alpha ethyltryptamine (AET)	bufotenine
diethyltryptamine (DET)	dimethyltryptamine (DMT)
KETAMINE	lysergic acid diethylamide (LSD)
mescaline	peyote
PHENCYCLIDINE (PCP)	psilocybin

See also CLUB DRUGS; ILLICIT DRUG USE; HYPNOTICS; NEURON; NEUROTRANSMITTER; SCHEDULED DRUGS; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

hangover Unpleasant physical symptoms that occur as a toxic reaction after excessive consumption of ALCOHOL. These symptoms are most prominent immediately on waking in the morning and may include

- significant HEADACHE
- NAUSEA
- VOMITING
- dizziness and VERTIGO
- PHOTOPHOBIA (aversion to bright light)

Though many remedies profess to prevent or cure hangover, the only prevention is avoiding excessive alcohol consumption and the only cure is time. The folk remedy of consuming an alcoholic drink to relieve hangover does not really end the hangover but instead induces mild INTOXICATION. In a person who is addicted to alcohol (ALCOHOLISM) this restores the effect of alcohol on the balance of neurotransmitters in the BRAIN. However, hangover is an indication that the LIVER's METABOLISM of alcohol has not been able to keep pace with the body's consumption, allowing higher concentrations of aldehyde (a toxin that is the first step of alcohol metabolism) to circulate in the BLOOD. There is some evidence that the herb MILK THISTLE (silymarin) improves liver function so the liver can more efficiently metabolize alcohol.

See also DETOXIFICATION; LIVER DISEASE OF ALCOHOLISM; WITHDRAWAL SYNDROME.

hashish See CANNABIS.

hash oil See CANNABIS.

heroin A narcotic DRUG derived from morphine. Widely used to relieve PAIN when it first became available in the early 1900s, heroin even appeared in over-the-counter pain remedies (as did other OPIATES) marketed to relieve various aches and discomforts. Today, however, heroin has no therapeutic uses and is a schedule 1 drug in the United States, making it legally available only for clinical research. Heroin has very high risk for DEPENDENCE and ADDICTION; heroin addiction presents significant health and social problems in the United States and throughout the world.

Heroin absorbs poorly through the gastrointestinal mucosa; thus its classic method of administration is intravenous injection (injected with a

needle directly into a VEIN). Other means of using heroin are injecting it—intramuscular (into a MUSCLE) or under the SKIN (subcutaneous, also called "skin popping")—snorting it into the NOSE, or smoking it mixed with tobacco or marijuana. These other methods are no less addictive, though snorting and smoking do reduce the risk for contracting bloodborne diseases such as HEPATITIS and HIV/AIDS. Such infections are significant risks with injected drugs of abuse, particularly when users share needles, syringes, and other paraphernalia.

The risk for OVERDOSE is high because heroin's potency and other ingredients are uncertain from DOSE to dose. Most powder sold as heroin is 10 to 70 percent heroin. The remainder may be other number of other substances from sugar to acetaminophen to other illicit drugs or even poisons. Exceptionally pure heroin is also hazardous because it is more narcotic than the person is accustomed to using.

HEALTH RISKS OF HEROIN ABUSE

Short Term	
CONSTIPATION	delayed reactions
drowsiness	inability to concentrate
NAUSEA and VOMITING	OVERDOSE
Long Term	
ADDICTION	ENDOCARDITIS and other bacterial INFECTION
HEPATITIS, HIV/AIDS, and other viral infection	scarring and damage to BLOOD vessels

See also INJECTING DRUGS, RISKS OF; NARCOTICS; SCHEDULED DRUGS; SMOKING AND HEALTH; WITHDRAWAL SYNDROME.

hypnotics DRUGS that induce sleep or cause heavy sedation. Hypnotics are CENTRAL NERVOUS SYSTEM DEPRESSANTS that act primarily to elevate levels of gamma aminobutyric acid (GABA), a NEUROTRANSMITTER that conveys NERVE impulses among BRAIN neurons to slow brain activity. BARBITURATES, most BENZODIAZEPINES, and some ANTIHISTAMINE MEDICATIONS have hypnotic actions.

Short-term health risks of hypnotic use include

- excessive drowsiness or difficulty waking up in the morning
- sense of sluggishness the next day

These consequences and side effects usually go away after the drug is no longer present in the body. Health risks of continued or long-term use of hypnotics may include

- DEPENDENCE on the drug to fall asleep
- ADDICTION
- severe withdrawal symptoms when suddenly stopping the drug, including possible PSYCHOSIS
- profound DEPRESSION
- increased potential for OVERDOSE

Because the body develops TOLERANCE for hypnotics, the margin between a safe amount of the drug and the amount necessary to produce the desired effect narrows with long-term use. This is particularly hazardous with barbiturates and can result in unintended fatal overdose.

COMMON HYPNOTICS

BARBITURATES	BENZODIAZEPINES
CHLORAL HYDRATE	diphenhydramine
doxcylamine	ethchlorvynol
GAMMA HYDROXYBUTYRIC ACID (GHB)	GLUTETHIMIDE
meprobamate	methaqualone
METHYPRYLON	paraldehyde
zaleplon	zolpidem

See also SCHEDULED DRUGS; SLEEP DISORDERS; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

I

illicit drug use Any use of substances not legal to possess. Many illicit drugs are "underground" drugs that individuals manufacture specifically for illicit use. Some of these drugs may be legal in other countries though are not legal in the United States or in the country in which the person is using them. As well, illicit drugs may be drugs that are legal but the person possessing them does not have legal authorization, such as a physician's prescription.

A significant health concern with illicit drugs is their production. Many drugs that come in loose form (such as HEROIN, COCAINE, METHAMPHETAMINE, and marijuana) are "cut" with various and often unknown substances, including other drugs and sometimes chemicals not intended for human consumption. These fillers, which dilute the DRUG's strength, may alter the actions of the drug or themselves cause effects in the body that are unexpected or toxic. The manufacture of illicit drugs in pill form is also questionable, with potency and ingredients varying certainly from batch to batch and often from pill to pill. Many people who manufacture illicit drugs such as methamphetamine have little knowledge of chemistry beyond that required to produce the drugs, and produce the drugs in less than ideal and often unsanitary conditions.

Other illicit drugs are produced in countries where their use is legal; they are smuggled into the United States and other countries. The production circumstances may or may not be of acceptable standards in terms of the drug's purity and consistency and the cleanliness of the manufacturing environment. Manufacturing inconsistencies, sanitation, and impurities may all pose health risks for people who use drugs smuggled into the United States from other countries. The other significant risk with illicit drugs is the legal consequence for their possession, which may result in jail sentences, fines, and serious consequences for a person's career, family, and lifestyle. In the United States the 1970 Controlled Substances Act (CSA) and its subsequent revisions establish the legality of drugs. Other countries have comparable legislative guidelines.

COMMONLY ABUSED ILLICIT DRUGS

ANABOLIC STEROIDS AND STEROID PRECURSORS	COCAINE
	FLUNITRAZEPAM
GAMMA HYDROXYBUTYRIC ACID (GHB)	hashish
	HEROIN
LSD	marijuana
mescaline	METHAMPHETAMINE
METHYLENEDIOXYMETHAMPHETAMINE (MDMA)	peyote

See also ADDICTION; CLUB DRUGS; DESIGNER DRUGS; STIMULANTS; HALLUCINOGENS; NARCOTICS; OPIATES; PRESCRIPTION ABUSE; SCHEDULED DRUGS; SUBSTANCE ABUSE PREVENTION.

injecting drugs, risks of The potential health consequences of sharing needles and DRUG paraphernalia. Sharing needles allows the passing of BACTERIA and viruses that are in the BLOOD among all individuals who use the needles. Rinsing with water or cleaning with bleach is not enough to prevent INFECTION with many bloodborne pathogens.

Intravenous drug users who share needles and drugs have particularly high risk for infection with bloodborne viruses such as HEPATITIS B, hepatitis C, HIV/AIDS, and for acquiring bacterial infections such as TUBERCULOSIS and MENINGITIS. It is also possible to acquire infection with some SEXUALLY TRANSMITTED DISEASES (STDS).

Needle exchange programs have become effective public health tools for reducing communicable disease transmission among intravenous drug users. Local health departments administer such programs, which give the person a sterile needle and syringe in exchange for a used one. Though it is a common perception that such needle exchange programs inherently encourage intravenous drug abuse, there is little clinical evidence that this is the case. Many substance abuse experts believe needle exchange programs, though they do not overtly encourage users to stop using drugs, do provide regular access to information about treatment programs that allow users who want to stop to find the help they need to do so as well as reduce the risk for disease.

See also SEXUAL HEALTH; SEXUALLY TRANSMITTED DISEASE (STD) PREVENTION; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

intoxication The presence of ALCOHOL or other DRUG in the body in an amount that alters perception, behavior, thought processes, motor skills, judgment, and other physical or psychologic activities in ways that are dysfunctional or disruptive. From a health perspective intoxication is a state of poisoning. Slang terminology for intoxication includes drunkenness (alcohol intoxication), stoned, high, and buzzed. The primary objective of substance abuse is to achieve a state of intoxication, which continues for as long as the substance responsible for it remains active in the body. In the United States and most countries laws define the legal boundaries of intoxication, beyond which intoxication while participating in certain activities such as driving becomes a criminal offense.

See also DETOXIFICATION; ILLICIT DRUG USE; OVERDOSE; POISON PREVENTION; PRESCRIPTION DRUG ABUSE; SOBRIETY; SUBSTANCE ABUSE TREATMENT.

K–M

ketamine An intravenous anesthetic agent used primarily in veterinary medicine that has euphoric and hallucinogenic effects when used as a substance of abuse. Ketamine causes a sense of dissociation (separation of one's self from PAIN and other physical sensations associated with surgery), amnesia for events that occur while it is effective in the body, and primarily visual HALLUCINATION that are often quite vivid. Users sprinkle ketamine powder on cigarettes or marijuana and smoke it, snort the powder, or dissolve the powder and inject it intravenously. Excessive doses result in anesthesia-like loss of CONSCIOUSNESS. In the United States ketamine is a schedule 3 drug.

See also ANESTHESIA; CANNABIS; ILLICIT DRUG USE; NARCOTICS; PHENCYCLIDINE (PCP); SCHEDULED DRUGS.

levo-alpha acetylmethadol (LAAM) An oral DRUG to treat narcotic ADDICTION, primarily HEROIN addiction. LAAM is a synthetic product similar in chemical composition as well as action in the body to METHADONE, though a single DOSE is effective for up to 72 hours. In the United States LAAM is a schedule 2 drug. However, a rare but serious SIDE EFFECT of LAAM is damage to the HEART and BLOOD vessels. Because of this, doctors use LAAM primarily when treatment with methadone is not effective.

See also NALTREXONE; SCHEDULED DRUGS; SUBSTANCE ABUSE TREATMENT.

LSD See HALLUCINOGENS.

marijuana See CANNABIS.

methadone A synthetic analgesic (PAIN medication) originally developed as an oral substitute for morphine, a narcotic analgesic, during World War II. Methadone binds with opiate receptors in the BRAIN in the same way as does morphine, though methadone's chemical structure differs from that of morphine and methadone's effects last up to 24 hours.

Methadone has similar risk as OPIATES for DEPENDENCE and ADDICTION. In the United States methadone is a schedule 2 DRUG doctors prescribe primarily to treat HEROIN addiction. It works by blocking opiate receptors in the brain, which prevents other opiates such as heroin from doing so. Though methadone is itself addictive, withdrawal symptoms are less severe than withdrawal from heroin. As a drug of abuse methadone has effects similar to those of heroin. Doctors also occasionally prescribe methadone as an analgesic, often to treat CHRONIC PAIN.

See also ANALGESIC MEDICATIONS; DETOXIFICATION; ILLICIT DRUG USE; SCHEDULED DRUGS; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

methamphetamine A very potent DRUG that is a CENTRAL NERVOUS SYSTEM stimulant. Though one formulation of methamphetamine is available for therapeutic use to treat a certain type of NARCOLEPSY, in the United States methamphetamine is primarily illicit and classified as a schedule 2 drug; its possession and therapeutic uses are extremely limited. Highly addictive, methamphetamine produces euphoria and a sense of invincibility. The drug stays active in the body for an extended time, making repeated use dangerously toxic; fatal OVERDOSE is a significant risk.

Though relatively simple from a chemistry perspective, which gives rise to proliferate clandestine "meth labs," the manufacture of methamphetamine is also quite toxic. Meth labs require only rudimentary equipment and supplies. However, the methamphetamine production process is so

harmful that it renders uninhabitable or unusable any structures (including homes, apartments, and motels) used for meth labs.

Chronic, long-term methamphetamine abuse causes serious and permanent damage to many body systems. Classic indications of such abuse include rotted and missing TEETH, emaciated appearance, open sores on the face, and patchy HAIR loss. Continuous picking at the SKIN reflects damage to BRAIN neurons; PARANOIA and SCHIZOPHRENIA are common with chronic methamphetamine abuse. DETOXIFICATION and maintaining SOBRIETY are difficult.

HEALTH RISKS OF METHAMPHETAMINE ABUSE

Short Term

altered reactions and reaction time	disordered thinking
excitability and hyperactivity	DYSPHORIA as effect wears off
unpredictable and violent behavior	rapid mood swings

Long Term

ADDICTION	HALLUCINATION
MALNUTRITION	PSYCHOSIS
rotted TEETH	SCHIZOPHRENIA
sores on the face and body	unhealthy weight loss

See also HALLUCINOGENS; ILLICIT DRUG USE; SCHEDULED DRUGS; STIMULANTS; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

methylenedioxymethamphetamine (MDMA) An illicit DRUG that acts on the CENTRAL NERVOUS SYSTEM to produce hallucinogenic and stimulant effects. A designer drug, MDMA is best known by its slang name ecstasy. MDMA is chemically similar to amphetamine, a stimulant, and mescaline, a hallucinogen. The drug's risks for DEPENDENCE and ADDICTION are very high. In the United States MDMA is a schedule 1 drug with no therapeutic uses.

The desired effects of MDMA are euphoria, increased energy, heightened sensory perceptions, and intensified sexual interest and experiences. The undesired side effects of MDMA may have long-lasting or permanent consequences, including ARRHYTHMIA, organ damage or failure, and damage to BRAIN neurons. Cravings for MDMA can continue long after stopping the drug. As well, because MDMA is an illicit drug it is often contaminated with other drugs, commonly amphetamine compounds, though underground chemists use a variety of substances as fillers. These substances may interact with each other or have toxic consequences of their own.

HEALTH RISKS OF MDMA (ECSTASY) ABUSE

Short Term

disturbed thought processes	erratic body temperature
HYPERTENSION	hyperthermia
increased or irregular HEART RATE (ARRHYTHMIA)	memory impairment

Long Term

ADDICTION	BRAIN damage
cognitive dysfunction	organ damage

See also AMPHETAMINES; CLUB DRUGS; COGNITIVE FUNCTION AND DYSFUNCTION; HALLUCINOGENS; MEMORY AND MEMORY IMPAIRMENT; NEURON; SCHEDULED DRUGS; STIMULANTS; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

N

naltrexone A medication to treat opiate ADDICTION. Naltrexone binds with opiate receptors in the BRAIN, preventing opiate drugs from binding. This action can block further effect of OPIATES already in the body or prevent the effect of opiates taken after naltrexone is in the body. Naltrexone is a treatment for addiction to opiates including prescription NARCOTICS and illicit drugs such as HEROIN. Naltrexone also helps reduce ALCOHOL cravings in some people who are recovering from ALCOHOLISM. Naltrexone is most effective in people who have strong desire to remain abstinent from DRUG or alcohol use and when starting DETOXIFICATION as part of a comprehensive SUBSTANCE ABUSE TREATMENT program.

See also ILLICIT DRUG USE; LEVO-ALPHA ACETYLMETHADOL (LAAM); METHADONE; PRESCRIPTION DRUG ABUSE; WITHDRAWAL SYNDROME.

narcotics Drugs that produce insensitivity to physical sensation, often altering perception and the level of CONSCIOUSNESS. Many narcotics subject to abuse are legitimate drugs that have therapeutic uses such as to relieve PAIN, stop COUGH, and treat DIARRHEA. Anesthesiologists use some narcotics to initiate or provide ANESTHESIA. Some narcotics are illicit, produced in clandestine labs by people who have rudimentary knowledge of chemistry. All narcotics have high risk for DEPENDENCE and ADDICTION. Accordingly narcotics are SCHEDULED DRUGS in the United States and many other countries, restricting their legal use and possession.

Narcotics act on neuroreceptors in the CENTRAL NERVOUS SYSTEM (BRAIN and SPINAL CORD) called opiate receptors, which researchers discovered in 1973. These specialized proteins regulate the brain's perceptions about and responses to pain signals as well as certain aspects of mood and consciousness. Opiate receptor binding also influences the rate of BREATHING (respiratory rate). The gastrointestinal tract contains some opiate receptors, which is why certain types of narcotics are useful for treating diarrhea and others cause CONSTIPATION as an undesired SIDE EFFECT.

There are two general classifications of narcotics: OPIATES, which come from natural sources, and synthetics, which are produced from chemicals in laboratories. Opiates derive from opium, the sap from the *Papaver somniferum* poppy plant. Synthetic narcotics, sometimes called opioids because they act in an opiate-like manner in the body, are chemical formulas designed in the laboratory to bind with specific types of opiate receptors for a lower risk of dependence and addiction. Opiate receptors rapidly become tolerant to the actions of narcotics, resulting in higher doses being necessary to achieve the same effect.

Narcotics come in forms for all ROUTES OF ADMINISTRATION: oral (liquids, tablets, capsules), rectal (suppositories), sublingual (under the tongue), intravenous injection (with a needle into a VEIN), intramuscular injection (with a needle into a MUSCLE), subcutaneous (with a needle under the SKIN), transdermal (patches, for absorption through the skin), and mucosal (sprays or lozenges, for absorption through the mucous membranes of the MOUTH or NOSE). Some narcotics do not absorb well through the gastrointestinal tract and are available only for injection, whereas for other narcotics injection offers the most rapid effect. The most commonly used methods for abuse are oral and injectable. As well, in circumstances of narcotic abuse a person may add a powdered narcotic to a

cigarette and smoke it, which allows absorption through the LUNGS.

The short-term health risks of narcotic use include

- drowsiness
- reduced alertness or consciousness
- NAUSEA, VOMITING, and constipation

Health risks that may occur with long-term use of narcotics include

- TOLERANCE, dependence, and addiction
- INFECTION through shared needles among those who inject the drugs
- depressed respiration and RESPIRATORY FAILURE leading to death as the boundary between effective and toxic dosages grows increasingly narrow

Narcotic antagonists are drugs that have greater affinity for opiate receptors than do narcotics; they are able to "bump" opioids from the receptors. These drugs are often effective for treating narcotic OVERDOSE and addiction. DETOXIFICATION from narcotic addiction often entails numerous withdrawal symptoms that are more severe the longer a person has taken or abused the drugs.

COMMON NARCOTICS

Opiates (Narcotics of Natural Origin)	
codeine	HEROIN
hydrocodone	hydromorphone
morphine	oxycodone
paregoric (opium)	thebaine
Synthetics (Opioids)	
BUPRENORPHINE	butorphanol
dextropropoxyphene	fentanyl
meperidine	METHADONE
pentazocine	

See also ANALGESIC MEDICATIONS; ILLICIT DRUG USE; NARROW THERAPEUTIC INDEX (NTI); PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

needle exchange programs See INJECTING DRUGS, RISKS OF.

nicotine The primary psychoactive DRUG in tobacco and SMOKING CESSATION products. Nicotine has stimulant as well as vasoconstrictive effects and is highly addictive. Many health experts consider nicotine at least as addictive as COCAINE and HEROIN. Most tobacco users, particularly smokers, attempt to quit numerous times before they achieve long-term success. Nicotine crosses the BLOOD–BRAIN BARRIER within seconds of tobacco use, where it affects the presence and activity of several BRAIN neurotransmitters, notably DOPAMINE and acetylcholine. These actions set in motion a cascade of events throughout the body that affect multiple functions, ranging from mood to cardiovascular activity.

Common sources of nicotine include

- cigarettes
- cigars
- NICOTINE REPLACEMENT products
- smokeless (chewing) tobacco
- snuff

HEALTH RISKS OF NICOTINE ABUSE

Short Term
activation of STRESS RESPONSE HORMONAL CASCADE
elevated BLOOD PRESSURE
increased HEART RATE
vasoconstriction
Long Term
ADDICTION
ARTERIOSCLEROSIS
chronic HYPERTENSION
health complications associated with tobacco use
inability to focus without nicotine in the BLOOD circulation

As a stimulant nicotine can heighten a person's mental focus and cognitive capability. However, tolerance develops rapidly such that with continued use (nicotine ADDICTION) this effect diminishes. Nicotine, through its effect on acetylcholine in the brain, activates the STRESS RESPONSE HORMONAL CASCADE, increasing the flow of EPINEPHRINE and NOR-

EPINEPHRINE in the body. This causes immediate changes in the walls of the arteries, causing them to stiffen and narrow. With long-term use of nicotine-containing substances these changes become permanent and alter cardiovascular function, contributing to serious HEART conditions such as HYPERTENSION (high BLOOD PRESSURE) and HEART FAILURE. The cardiovascular changes also affect the body's tiniest arteries, which can result in restricted circulation in the fingers and toes (RAYNAUD'S SYNDROME) and of the blood flow to the PENIS, resulting in ERECTILE DYSFUNCTION. The only therapeutic use for nicotine is in nicotine replacement products to treat nicotine addiction (SMOKING CESSATION).

See also ANTISMOKING EFFORTS; CANCER RISK FACTORS; CARCINOGEN; ENVIRONMENTAL CIGARETTE SMOKE; NEUROTRANSMITTER; SMOKING AND CANCER; SMOKING AND CARDIOVASCULAR DISEASE (CVD); SMOKING AND HEALTH; WITHDRAWAL SYNDROME.

O–R

opiates Drugs derived from opium, the dried sap of the *Papaver somniferum* poppy plant. *P. somniferum* is the only one of about 120 species in the *Papaver* family of poppy plants that produces opium; other species are common ornamental flowering annuals or perennials. In the United States opiates are SCHEDULED DRUGS, restricting legal use and possession to physician prescription. HEROIN, which derives from morphine, is a schedule 1 drug, a classification that prohibits possession and use. Opiates have moderate to high risk for TOLERANCE, DEPENDENCE, and ADDICTION.

Most opiates are NARCOTICS used for analgesia (PAIN relief) or ANESTHESIA (loss of sensation). Opium is the main ingredient in the medication paregoric, sometimes used to treat DIARRHEA. Because opiates suppress the COUGH REFLEX, prescription antitussive medications often contain them (notably codeine and hydrocodone). The most effective opiate for significant pain relief, such as pain after surgery or terminal pain, is morphine, which became available in sustained-release tablets in the 1990s. The most commonly used opiates are hydrocodone and codeine, which appear in numerous products to relieve moderate pain and also for cough relief.

COMMON OPIATES

alfentanil	butorphanol
codeine	dextropropoxyphene
fentanyl	HEROIN
hydrocodone	hydromorphone
meperidine	METHADONE
morphine	oxycodone
pentazocine	sufentanil

See also ANALGESIC MEDICATIONS; DEXTROMETHORPHAN; ILLICIT DRUG USE; INJECTING DRUGS, RISKS OF; LEVO-ALPHA ACETYLMETHADOL (LAAM); NALTREXONE; PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

organic solvents Petroleum distillates found in gasoline and some paints, paint thinners, aerosols, household cleaners, and glues. When inhaled in small quantities organic solvents produce a sense of INTOXICATION and mild HALLUCINATION. Inhaling the vapors into the LUNGS allows rapid absorption into the BLOOD circulation. However, the margin between intoxication and neurologic toxicity is very narrow and inhaled solvents can cause rapid death. The highest rate of organic solvent abuse is among children between 9 and 13 years of age.

Short-term health risks of inhaling organic solvents include

- slurred speech and uncoordinated movement
- HEADACHE
- NAUSEA and VOMITING
- panic attacks
- erratic mood and behavior
- DEPRESSION
- ASPIRATION of the substance into the lungs
- asphyxiation (suffocation) resulting in death

Long-term abuse of inhalants has significant health risks including

- RENAL FAILURE
- LIVER damage
- cognitive dysfunction
- memory impairment
- HEART FAILURE

Because numerous products contain organic solvents, preventing inhalant abuse is challenging. The very fact that these products are ordinary and common perpetuates the mistaken belief that inhaling them is harmless. Many parents are unaware of the practice of sniffing or huffing such products. Substance abuse experts urge parents to read product labels to identify those products that contain organic solvents to minimize the amount of such products in the home. Indications a child may be abusing substances containing organic solvents include

- RASH around the NOSE and MOUTH
- wheezing and coughing (new and unrelated to upper respiratory INFECTION)
- red, teary eyes
- unpredictable and erratic behavior

COMMONLY ABUSED ORGANIC SOLVENTS

acetone	benzene
methanol	methyl butyl ketone
methyl ethyl ketone	methylene chloride
toluene	trichloroethane
trichloroethylene	

See also ALKYL NITRITES; ILLICIT DRUG USE; PANIC DISORDER.

performance-enhancing substances Drugs, hormones, herbs, and nutritional supplements an individual takes to improve athletic capability or that results in an unfair competitive advantage. Performance-enhancing substances present health risks because they alter the body's functions or structure.

Athletic organizations in the United States and internationally prohibit the use of performance-enhancing substances at all levels of participation and competition, though the kinds of substances banned varies with the sport and level of competition. However, use and abuse of performance-enhancing substances remains a particular concern among younger athletes who compete at levels where testing for banned substances is infrequent or does not occur. PEER PRESSURE and perceptions that such substances are necessary to excel (win) may also be factors.

CAFFEINE is perhaps the most commonly used performance-enhancing substance. Coffee, tea, and cola drinks contain caffeine as do many energy drinks, gels, and food bars. Energy products also commonly contain GINSENG and other herbs that act as STIMULANTS. Some contain ma huang, a Chinese herb whose active ingredient is ephedra, a stimulant that is no longer legal in the United States. Other commonly available products used for their stimulant actions to enhance performance are decongestants such as pseudoephedrine. Illicit performance-enhancing substances include ANABOLIC STEROIDS AND STEROID PRECURSORS, ERYTHROPOIETIN (EPO), human growth hormone (hGH), and prescription stimulants.

See also BLOOD DOPING; DESIGNER DRUGS; HORMONE; MUSCLE.

phencyclidine (PCP) A veterinary anesthetic that causes varied and unpredictable effects when used as a substance of abuse. A single use may result in long-term psychiatric disorders such as PARANOIA, PSYCHOSIS, mood disorders, and SCHIZOPHRENIA. Though the risks for DEPENDENCE and ADDICTION are high with chronic use, the unpredictability and unpleasantness of PCP's effects tend to limit its use. PCP is a schedule 2 drug in the United States. However, no manufacturers currently produce it so it is nearly always an illicit drug. The most common method of use is to sprinkle the powder on a cigarette or onto marijuana and smoke it.

HEALTH RISKS OF PHENCYCLIDINE ABUSE

Short Term	
amnesia	dissociation
extreme anxiety	HALLUCINATION
involuntary MUSCLE activity	loss of physical coordination
slurred speech	violent behavior
Long Term	
GENERALIZED ANXIETY DISORDER (GAD)	mood disorders
PARANOIA	movement disorders
SCHIZOPHRENIA	PSYCHOSIS

See also ILLICIT DRUG USE; HALLUCINOGENS; KETAMINE; STIMULANTS; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

prescription drug abuse The misuse of drugs prescribed for therapeutic purposes. Most prescription DRUG abuse begins unintentionally and may become intentional as psychologic DEPENDENCE or ADDICTION develops. The most commonly abused prescription drugs are NARCOTICS, BENZODIAZEPINES, and STIMULANTS. In the context of abuse, possession and use of the drugs may be illicit when the means of obtaining the drugs is illicit, such as through altered or forged prescriptions, or obtaining drugs through unlicensed sources.

See also ANALGESIC MEDICATIONS; ILLICIT DRUG USE; OPIATES; SCHEDULED DRUG; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

Rohypnol See FLUNITRAZEPAM.

S

sobriety The state of abstinence from ALCOHOL and drugs. Sobriety is a marker of success in SUBSTANCE ABUSE TREATMENT. Individuals who are in recovery keep track of the length of time they remain sober. When treatment and sobriety are ordered through the courts, such as in connection with the breaking of laws in regard to use or possession of alcohol or drugs, it may be necessary for the person to prove sobriety through BLOOD and URINE tests that check for the presence of prohibited substances. Sobriety begins when the body is clear of alcohol or drugs, which may take days to weeks, depending on the substance, and continues for as long as it remains so.

See also DETOXIFICATION; ILLICIT DRUG USE; INTOXICATION; PRESCRIPTION DRUG ABUSE.

stimulants Drugs that stimulate the CENTRAL NERVOUS SYSTEM, producing heightened awareness and alertness. Stimulants have therapeutic uses as treatments for ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD), NARCOLEPSY, sinus congestion, and weight loss. All central NERVOUS SYSTEM stimulants belong to the same general DRUG classification, sympathomimetic amines, and elicit the same kinds of responses though at varying levels. Stimulants have moderate to high risk for DEPENDENCE and ADDICTION.

Over-the-Counter Stimulants

Numerous stimulants are commonly available without a doctor's prescription, such as

- CAFFEINE, found in coffee, tea, cola, and energy drinks, gels, and food bars as well as in OVER-THE-COUNTER (OTC) DRUGS for weight loss, alertness, and PAIN relief
- NICOTINE, the primary active ingredient of tobacco
- pseudoephedrine and phenylephrine, decongestants found in OTC cold remedy and allergy relief products
- GINSENG, guarana, and kola nut, which are common ingredients in energy products

Though OTC and herbal products containing stimulants are readily available, they are not inherently safe. Herbal products, which are not subject to regulation as drugs in the United States, often contain numerous and sometimes poorly identified ingredients that may interact with each other or are of inconsistent potency and purity. Ephedrine and phenylpropanolamine are formerly common decongestants that are now banned in the United States, though herbal products manufactured in other countries sometimes contain them. Ma huang, a common Chinese herb, is a natural source of ephedra, an ephedrine alkaloid. Many states also limit the sale of pseudoephedrine, once the most commonly used decongestant, because of its use in illicitly manufacturing METHAMPHETAMINE, to which it has key chemical similarities.

Prescription and Illicit Stimulants

Federal law in the United States regulates most stimulant drugs as SCHEDULED DRUGS; possession and use require a physician's prescription. Prescription stimulants most commonly abused include AMPHETAMINES, dextroamphetamine, and methylphenidate. Illicit stimulants most commonly abused are COCAINE and METHAMPHETAMINE. These drugs all have high risk for psychologic dependence and addiction as well as for with-

drawal symptoms when stopping them. A unique risk of cocaine use is that of SUDDEN CARDIAC DEATH due to the drug's unpredictable effects on the HEART and cardiovascular system.

COMMON STIMULANTS

AMPHETAMINES	benzphetamine
CAFFEINE	COCAINE
dextroamphetamine	diethylpropion
ephedra	ephedrine
mazindol	METHAMPHETAMINE
methcathinone	methylphenidate
modafinil	NICOTINE
phendimetrazine	phentermine
phenylephrine	pseudoephedrine

See also ILLICIT DRUG USE; PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

substance abuse treatment A method for helping people stop abusing drugs (including ALCOHOL), overcome ADDICTION, and maintain SOBRIETY. The acute stage of substance abuse treatment is DETOXIFICATION, which is most often a health circumstance that requires medical care until the person's body is completely free from the drug (typically 72 hours to 10 days). This stage of treatment is often inpatient though may be outpatient.

The follow-up treatment may last weeks to months, depending on the nature of the addiction and the person's individual situation. This stage may have require inpatient treatment with follow-up outpatient care or may be entirely outpatient. There are numerous methods for substance abuse treatment. The two main structured approaches are the 12-step programs and BEHAVIOR MODIFICATION THERAPY.

12-Step Programs

The original 12-step program, started in the 1930s, is Alcoholics Anonymous, which today has more than two million members worldwide. As well there are numerous similar programs for other addictions. The basic premise of the 12-step program is that addiction is an incurable disease from which a person is in ongoing recovery no matter how long he or she has maintained sobriety.

A fundamental tenet of the 12-step approach is anonymity for members within a structure of regular meetings that provide consistent peer support. There are no requirements for membership in 12-step groups other than agreement to follow the 12 steps; and there are no fees, charges, or dues. Each group determines the ways in which its members support the group's functions and expenses. There are also 12-step support programs, such as Al-Anon, for the family members and friends of people who have addictions.

Behavior Modification Therapy

Behavior modification therapy is formally structured care through a licensed psychologist or substance abuse professional and takes the approach that a person can change the ways he or she thinks and acts in regard to alcohol and drugs of abuse. Methods may include incentives, setting and then working to meet goals, behavior substitution skills, PSYCHOTHERAPY to help the person understand his or her reasons for abusing drugs or alcohol, education about drugs and addiction, and techniques for coping with situations that present high risk for relapse. Behavior modification therapy builds on the premises that the individual is responsible for his or her behavior, behaviors are learned, and learning new behaviors is always possible.

Related Health Care and Lifestyle Issues

Many people recovering from addiction have other health conditions that need appropriate medical attention, from NUTRITIONAL DEFICIENCY to damage resulting from abused drugs or alcohol. Recovery from substance abuse must also include treatment for such health conditions. Some conditions, such as HEPATITIS or other bloodborne infections, may require medications or extended treatment. Other conditions, such as LIVER disease or CARDIOVASCULAR DISEASE (CVD), may need ongoing medical care.

Nutritional eating is particularly important because nutritional deficiencies are common. Many people need vitamin and mineral supplements. Eating foods that are enjoyable provide a source of pleasure. Regular physical exercise is also important to maintain overall health as well

as help stabilize mood, reduce cravings for drugs or alcohol, and provide a sense of purpose and routine.

Long-Term Outlook

Though many people successfully maintain sobriety and a drug-free lifestyle, relapse into addiction is not uncommon. Maintaining sobriety is an ongoing effort that requires continuous attention that many people find more challenging than they can manage. The more skills a person acquires for finding alternatives to drugs and alcohol—jobs, education, community involvement, sports and athletics, and other activities that provide a productive, fulfilling experience of everyday life—the more likely he or she will also create long-term success with treatment.

Support from family members and friends is also essential. Many people who relapse do so because they do not separate from the circumstances and relationships that supported their addictions. Underlying or co-existing psychiatric disorders or psychologic conditions often contribute to relapse. When considering and evaluating potential substance abuse treatment programs, it is important to ask what about the program's rate of success and how the program measures it.

See also ALCOHOLISM; EXERCISE AND HEALTH; ILLICIT DRUG USE; NUTRITION AND HEALTH; PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE PREVENTION; SUPPORT GROUPS.

T–W

tobacco A plant cultivated as a crop in the southern United States and regions around the world with similar climate. In the United States federal and state laws regulate the sale and possession of tobacco products, with most states restricting sales to people age 18 or older (age 19 in a few states). Further restrictions on smoking affect the use of tobacco throughout the United States.

Though tobacco releases hundreds of chemicals when it burns, its primary psychoactive ingredient is NICOTINE, a powerful stimulant and vasoconstrictor (narrows and stiffens the BLOOD vessels). Nicotine enters the blood circulation within seconds of the first inhalation of cigarette smoke and remains active in the body for up to two hours after the person finishes smoking the cigarette. Its primary route is via absorption in the LUNGS, though the mucous membranes of the MOUTH (oral mucosa) and NOSE also absorb nicotine from the smoke. Mucosal absorption is the primary route for nicotine and tobacco's other chemicals to enter the blood circulation with cigar smoking and forms of tobacco other than cigarettes, such as chewing tobacco and snuff.

No form of tobacco or tobacco product is safe to use. Any use of tobacco, smoked or oral, can cause numerous health conditions. Smoking tobacco further exposes others to health risks.

Nicotine is one of the most addictive substances known. It rapidly crosses the BLOOD–BRAIN BARRIER to act directly on neurotransmitters and neuroreceptors in the BRAIN, affecting primarily DOPAMINE and acetylcholine. Dopamine has numerous functions related to mood, emotion, and sensations of pleasure; researchers believe dopamine plays a key role in addiction not only to nicotine but to most psychoactive drugs. Acetylcholine affects the release of other neurotransmitters in the brain and hormones in the body, notably EPINEPHRINE and NOREPINEPHRINE. These chemicals stimulate brain activity as well as increase BLOOD PRESSURE and HEART RATE. Though cigarette smoking provides the most rapid release of nicotine with tobacco use, oral forms of tobacco (chewing tobacco and snuff) deliver significantly higher concentrations of nicotine into the blood circulation and thus have high risk for addiction though many people perceive them to have fewer health risks.

Dozens of the chemicals in tobacco are carcinogenic (cause cancer). Many are most potent when burning, such as smoking a cigarette or cigar, releases them. Tobacco use, primarily cigarette smoking, is the leading cause of CARDIOVASCULAR DISEASE (CVD), LUNG CANCER, laryngeal cancer, and CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). Chewing tobacco and snuff cause nearly all oral cancers (cancers of the mouth); cigar smoking also causes oral cancers. Smoked forms of tobacco also expose other people to carcinogenic chemicals.

See also ANTISMOKING EFFORTS; CANCER RISK FACTORS; CARCINOGEN; ENVIRONMENTAL CIGARETTE SMOKE; SMOKING AND CANCER; SMOKING AND CARDIOVASCULAR DISEASE (CVD); SMOKING AND HEALTH; SMOKING CESSATION; WITHDRAWAL SYNDROME.

tolerance The need for increasing amounts of a DRUG to reach the same level of effectiveness. Tolerance is an expected physiologic effect with many drugs; for some, the therapeutic benefits rely on it. Tolerance accounts for the ability of long-time users to take doses of drugs that might otherwise be harmful.

In the context of substance abuse, tolerance is a factor in the development of DEPENDENCE, in which body biochemistry changes in response to the drug's presence so that the body depends on the drug for a particular way of functioning, and in ADDICTION, in which the drive to use the drug (irrespective of dependence) is all-consuming so that most efforts in daily life focus on obtaining and using the drug. Dependence and addiction may have physiologic or psychologic components, or both; tolerance is physiologic and may occur without dependence or addiction.

Tolerance develops at an unpredictable rate with psychoactive drugs (drugs that affect the mind, mood, and emotions) and NARCOTICS. It may be necessary to wean from, or gradually taper the DOSAGE of, these drugs so a person may stop taking them without adverse effects.

See also DETOXIFICATION; ILLICIT DRUG USE; PRESCRIPTION DRUG ABUSE; SUBSTANCE ABUSE TREATMENT; WITHDRAWAL SYNDROME.

withdrawal syndrome The physical and psychologic symptoms that may occur with DETOXIFICATION from substance abuse, DEPENDENCE, or ADDICTION. The symptoms of withdrawal vary, depending on the substances of dependence and addiction. Because substance abuse often involves multiple drugs, there is wide variation in the specific symptoms individuals experience during detoxification. Among the more common symptoms are

- NAUSEA and VOMITING
- shivering or trembling ("the shakes")
- abdominal cramping or PAIN
- intense cravings for the drugs of abuse
- HALLUCINATION

ALCOHOL withdrawal, especially from long-term alcohol abuse, may result in DELIRIUM TREMENS, a severe and potentially fatal complex of symptoms that requires medical treatment and monitoring until the body completely detoxifies from alcohol. Withdrawal from BARBITURATES also requires close medical supervision and usually medications to relieve withdrawal symptoms; suddenly stopping barbiturates can result in lethal complications, resulting from NEUROTRANSMITTER imbalances in the BRAIN. Withdrawal from STIMULANTS typically causes profusely runny NOSE because stimulants have a decongestant action through constricting the BLOOD vessels in the nose. Withdrawal from OPIATES results in sometimes severe coughing because opiates suppress the COUGH REFLEX; removing this suppression causes rebound coughing until opiate receptors re-acclimate.

Doctors typically use medications such as BENZODIAZEPINES to ease withdrawal symptoms until detoxification is complete. Subsequent treatment to maintain SOBRIETY may include medications such as disulfiram and NALTREXONE for alcohol addiction and METHADONE, NALTREXONE, or LEVO-ALPHA ACETYLMETHADOL (LAAM) for narcotic addiction. Many people trying to stop smoking benefit from NICOTINE REPLACEMENT products to wean from NICOTINE addiction. When PRESCRIPTION DRUG ABUSE of NARCOTICS for CHRONIC PAIN relief results in dependence or addiction, subsequent treatment incorporates alternative methods of pain relief. Though withdrawal symptoms end when the substances of abuse are no longer present in the body, continued treatment for addiction remains key for preventing relapse.

See also ALCOHOLISM; ILLICIT DRUG USE; SMOKING CESSATION; SUBSTANCE ABUSE PREVENTION; SUBSTANCE ABUSE TREATMENT.

EMERGENCY AND FIRST AID

This section, "Emergency and First Aid," provides brief and basic instructional information for common health emergencies, directed at the average person who has minimal medical knowledge or training. The structure and presentation of the content in this section differs from other sections of *The Facts On File Encyclopedia of Health and Medicine* in having such an instructional focus. Other sections contain content that gives detailed information about the health conditions.

This content does not substitute for appropriate and timely medical attention from trained medical personnel. Nearly always, the most appropriate first step in an emergency is to call 911 to summon medical assistance.

Three basic rules govern emergency and first aid response for the average person in nearly every type of situation.

Rule One: First Summon Emergency Personnel

In the United States, cellular telephones and the 911 network have revolutionized emergency response. The first action for the first person on the scene of a medical emergency should be to call 911 to summon emergency medical personnel. If the responder does not have a cell phone odds are high that the person in need of assistance does; cell phones have become ubiquitous in American society. Except for the most remote areas, the 911 network coordinates response to all emergencies.

When calling 911 to report an emergency and request aid, certain basic information helps get the right assistance to the right location in the shortest amount of time.

- Where is the site or scene? If a home, provide the address. If a business, provide the name and address. When at a home or business, calling 911 from a land line (regular telephone) displays location information for 911 dispatchers. When at the scene of a traffic accident, try to note key location markers such as street names and intersections, highway numbers, exit ramp numbers, or milepost markers.
- What happened and is it still happening? Though most emergency dispatch includes law enforcement, fire, and medical personnel, knowing what has happened helps the 911 dispatcher send an appropriate balance and number of personnel. A motor vehicle accident, a fire, and a shooting situation require different blends of emphasis, personnel, and equipment.
- How many people are involved and what kinds of injuries or medical crises do they appear to have? Just the basics—bleeding, BURNS, HEART ATTACK, not BREATHING, not conscious—help the 911 dispatcher determine an appropriate level of medical response (evacuation helicopter or ambulance, for example).

Rule Two: Self-Protection

The natural tendency is to rush to provide assistance. But however strong the urge to leap into the situation, the first responder must not become another victim. Self-protection has two components: situational safety and personal safety.

Before moving to provide aid to the person in need, the responder must determine whether the situation continues to hold risk. If this is a fire, is it still burning? If a motor vehicle accident, is there traffic, are there downed power poles or trees, or are any of the involved vehicles unstable or at risk for fire? If an apparent heart attack, are there any indications of ELECTROCUTION such as power tools, electrical appliances, or downed power lines? Is there any evidence of toxic chemicals?

Next, the responder must protect his or her personal safety. This includes acting within the boundaries of personal expertise as well as safeguarding oneself from exposure to bloodborne pathogens. For example, a person who does not have training in water rescue should not enter the water to save someone who is drowning; being a strong swimmer is often not enough. Rushing into a burning building or automobile is heroic and may save a life otherwise lost; however, the risk is far greater that such action will result instead in losing another life. The success of such rescues often requires expertise, experience, and specialized equipment.

Exposure to pathogens through contact with body fluids is an unfortunately common means of contracting serious infections such as HEPATITIS, HIV/AIDS, and TUBERCULOSIS. Two essential items of personal protection that ideally all adults should have easily accessible are latex or latex-type gloves and CARDIOPULMONARY RESUSCITATION (CPR) shields. These items are widely available in disposable, key-chain-size packets. Medical response professionals encourage everyone to carry these two personal protection items in their vehicles, first aid kits, backpacks, purses, briefcases, or whatever they often have with them.

Rule Three: Do No Further Harm

Because emergency medical personnel can reach the scene of a medical emergency within minutes in most locations, often the most appropriate actions for the first responder to take are only those necessary to safeguard the person's life. Often the full extent of a person's injuries is not apparent.

For example, it is often better to leave a person injured in an auto accident in the vehicle until emergency personnel arrive, unless removing the person is essential to save his or her life. The tremendous forces of impact in MOTOR VEHICLE ACCIDENTS may cause head and SPINAL CORD trauma such that improperly moving the person could result in permanent PARALYSIS. As well, the pressure of being wedged in the vehicle may be containing an injury in ways that are temporarily beneficial, such as bracing a FRACTURE or slowing bleeding. Even an apparently obvious circumstance, such as near-drowning or heart attack, may have hidden injuries. More appropriate actions on the part of the first responder might be to turn off the vehicle's ignition and kick dirt or gravel over any gasoline or oil that has leaked from the vehicle, for example, or to cover the person with blankets or coats to keep him or her warm and dry.

Learn More

All teens and adults should receive emergency first aid and CPR training. Many high schools include these classes as part of the health curriculum. Many employers also provide such classes, often with content specific to health hazards encountered on-the-job. Public agencies in such as fire departments, police departments, public safety departments, health departments, community centers, and hospitals in most communities offer such classes for nominal or no cost.

Basic first aid and CPR are easy to learn; the investment of a few hours' time for classes may save countless lives. As well, many employers and public safety agencies conduct first responder training, typically a 40- to 60-hour curriculum that teaches advanced medical assistance and emergency response techniques. Companies and communities may then call on certified first responders in emergency situations.

First Response

The responses and actions of the first person who arrives on the scene of an emergency, commonly called the first responder, are crucial. This person must rapidly assess the nature of the situation, the safety of the site, and the possible injuries and treatment needs for those involved in the emergency. In many situations the most appropriate first response is to call 911 to summon medical assistance and provide comfort for those who are injured. In other circumstances the first responder may need to stop bleeding, perform CARDIOPULMONARY RESUSCITATION (CPR), or stabilize a possible FRACTURE.

The essential and most crucial first action for the first person to arrive on the scene of an emergency is to safeguard his or her own safety and protection. This means conducting a rapid but thorough SITE AND SITUATION ASSESSMENT to determine:

- What happened?
- Does the cause of the situation still exist as a risk for further harm?
- How many people appear to be involved?
- What is the nature of injuries or medical need?

The next action for the first responder is to summon aid. Though it is a natural tendency to rush to the aid of the person who needs care, the few seconds it will take to call 911 are more likely to save lives by getting trained and equipped rescue personnel to the scene. This is especially critical when the emergency is a HEART ATTACK; people who receive advanced cardiac care in a hospital within one hour of the heart attack's onset have a significantly higher chance of survival. As well, taking a few moments to survey the scene and the situation helps the responder focus and become calm.

The situation and circumstances determine the first responder's subsequent actions, which may include administering first aid, removing the person from danger, directing traffic or the activities of others who arrive to help, or simply comforting the person until medical and rescue personnel arrive. Because responding aid personnel may have questions about what happened or the circumstances under which the first responder happened upon the scene, the first responder should check with them before leaving the site.

body substance isolation Procedures for safely handling and disposing of body fluids and tissues such as BLOOD, SPUTUM, URINE, and feces. Body fluids can transmit bacterial and viral infections to others. Cuts and scrapes on the responder's body can allow pathogens to enter, risking INFECTION. Other possible points of entry are the responder's eyes, NOSE, and MOUTH.

Everyone who provides assistance to those who are injured or ill should wear latex or latex-type gloves and use barrier protection when performing resuscitation BREATHING to protect against direct contact with body fluids. Commercial first aid kits such as many people carry in their cars typically contain gloves. When gloves or resuscitation shields are not available, the responder must carefully consider his or her personal risk for infection before proceeding with any contact. The natural tendency when first arriving on the scene of an emergency to arrive at the scene of an emergency is to perform the necessary first aid procedures without consideration for personal risk. Materials such as clothing, towels, and other substances provide some protection from direct contact when the situation is life threatening. When emergency aid personnel are on the way a

minimal response may be both adequate and most appropriate.

Should direct contact with body fluids occur, the responder should wash the area of contact thoroughly (rinse extensively with water if the eyes or mouth) and promptly seek a doctor's advice and appropriate prophylaxis (preventive measures). Prophylaxis is available to reduce the risk for contracting infections such as HEPATITIS and TUBERCULOSIS. However, there are currently no methods to prevent infection with HIV (human immunodeficiency virus), the virus that causes AIDS (acquired immunodeficiency syndrome).

See also ACCIDENTAL INJURIES; BLEEDING CONTROL; CARDIOPULMONARY RESUSCITATION (CPR); HIV/AIDS; MULTIPLE TRAUMA; PATHOGEN; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

confidentiality The requirement to maintain the personal privacy of individuals who require emergency assistance or first aid. Though laws regarding confidentiality apply to people employed in fields such as health care, law enforcement, and firefighting, any person who responds to provide assistance should similarly respect the privacy of those involved in the situation. Such respect includes not discussing details of the situation with anyone, including media or press, other than those involved in the subsequent care of the person. A good rule of thumb is for the responder to consider whether he or she would want the information divulged were the responder the one who received assistance. As well, it is possible for there to be legal repercussions should information made public turn out to be erroneous.

See also GOOD SAMARITAN LAWS.

Good Samaritan laws Legal protections in the United States that states enact to shelter people who provide emergency assistance and first aid from legal liability for outcomes that may result from their actions. Such laws primarily affect individuals (other than those who work in public safety or health care jobs) who stop to help at MOTOR VEHICLE ACCIDENTS, when a person suffers a HEART ATTACK, or in other crisis situations. The premise is that the person providing aid is doing so with good intent and due prudence. These laws do not prevent legal action, however.

See also CONFIDENTIALITY; FIRST RESPONSE; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

responder safety and personal protection Items and methods responders should use when providing emergency assistance and first aid. The personal safety and protection of responders is essential. At a minimum, personal protection items should include

- latex gloves (or medical-grade, latex-free gloves for people who have latex allergies)
- a resuscitation shield or mask when performing RESCUE BREATHING or CARDIOPULMONARY RESUSCITATION (CPR)

Most commercial first aid kits now contain these items. If the responder does not have them, the person in need of medical attention might have them in a home or auto first aid kit. When these items are not available and the situation is a dire one in which the person is likely to die without immediate aid that risks exposure to body fluids, the responder can reduce such exposure by using clothing to establish a barrier.

The other fundamental dimension of responder safety and personal protection is quick but thorough SITE AND SITUATION ASSESSMENT to determine what, if any, risks exist that pose hazards for the responder. Key among these risks are the possibilities of

- fire, explosion, or ELECTROCUTION
- drowning, when the person needing assistance is in or near the water
- direct harm, when the situation is one of VIOLENCE such as a shooting
- hazardous conditions such as traffic or unstable terrain
- toxic chemical exposure

When these risks are present or uncertain, they put the responder at great peril.

See also ACCIDENTAL INJURIES; HEPATITIS PREVENTION; HIV/AIDS; INFECTION; PATHOGEN; SYMPTOM ASSESSMENT AND CARE TRIAGE; TUBERCULOSIS PREVENTION.

site and situation assessment The first action a responder should take when arriving at a situation that requires emergency assistance or first aid. The assessment must be brief but thorough enough to determine potential hazards for the responder as well as the condition of the person who needs assistance. Site and situation assessment should consider, at minimum

Nature of the emergency

- How many people are involved?
- Is anyone bleeding?
- Is anyone not BREATHING?
- Is the cause of the emergency still an active hazard?
- Are those who need aid safe from further harm?

Risk of fire

- Are flames visible?
- Is there a smell of smoke?
- Is there a smell of gasoline, diesel, oil, or natural gas?
- Are the engines of any vehicles still running after involvement in a collision or accident?
- Are there downed power lines?

Risk of ELECTROCUTION

- Are or were there power tools in use?
- Are there downed trees, power poles, or power lines?

Risk of drowning

- Is the person in water?
- Does the responder have training in water rescues?

Multiple hazards are often present, such as traffic attempting to pass through the scene of a motor vehicle accident or water on the surface when power lines are down. Less obvious hazards may include dogs in the home or at the scene of a motor vehicle accident whose behaviors to protect their owners threaten responders, power tools that have caused injury and remain plugged in, or gasoline leaking from a vehicle involved in an accident. Often the most appropriate response for the person first on the site is to summon emergency personnel and follow their instructions after they arrive for providing further assistance.

See also ACCIDENTAL INJURIES; MOTOR VEHICLE ACCIDENTS; RESPONDER SAFETY AND PERSONAL PROTECTION; SYMPTOM ASSESSMENT AND CARE TRIAGE.

symptom assessment and care triage A methodic approach to quickly determining the nature and severity of injuries so as to provide appropriate FIRST RESPONSE. A responder's ability to provide symptom assessment depends on the responder's level of knowledge and training.

Medical emergency personnel use various systems to triage patients—that is, determine the severity of injuries, type of care the injuries need, and likelihood for survival within the context of the medical resources immediately available. Emergency personnel will conduct such an assessment when they arrive at the site. In the meantime, the person who is first on the scene of a medical emergency that involves more than one person, or one person with multiple injuries, needs to determine how to provide the most appropriate attention to those who need care until medical emergency personnel arrive.

The most important and fundamental assessment is whether the person's life is in imminent danger. These four basic steps help make a rapid determination; the findings direct the responder's subsequent actions. Because time is crucial when the injuries or circumstances (such as HEART ATTACK) are life threatening, the basic assessment should take no more than 30 seconds.

1. **Is the person conscious?** If so ask, "Where do you hurt?" CONSCIOUSNESS, especially right after an injury or medical crisis such as heart attack, is not of itself an indication of whether the situation is life threatening.
2. **Is the person BREATHING?** Look for bluish gray discoloration of the lips, fingers, and SKIN overall. Watch to see if the person's chest rises and falls. Feel for air coming out of the NOSE or MOUTH.

3. **Is the person's HEART beating?** Feel for a PULSE in the side of the neck, two finger-widths below the notch toward the back of the lower jaw. Listen, with the EAR against the chest, for a heart beat.
4. **Is the person bleeding severely?** External bleeding is generally obvious; look at the person's front and back. Indications of internal bleeding include unusual or rapid swelling.

It is essential to assess all four life-threatening factors as well as the context of the situation before initiating emergency care because the findings determine the most appropriate response. Multiple life-threatening injuries present a complicated situation, especially when there is only one responder and he or she may have to make rapid decisions about what to do. It may be necessary to stop severe bleeding before proceeding to CARDIOPULMONARY RESUSCITATION (CPR), for example. The first action of the responder—call 911 to summon emergency aid—is often the most crucial.

See also BLEEDING CONTROL; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT.

Burns, Bleeding, Breaks

The most common types of injuries that require emergency medical assistance are BURNS, LACERATIONS (cuts) that result in external bleeding, BLUNT TRAUMA that results in internal bleeding, and fractures (broken bones). Many such injuries are mild to moderate in severity; mild burns and lacerations often require only self-care. Fractures and moderate injuries may need medical attention to assess their severity, especially burns and lacerations that may extend deep into the tissues.

Burns and bleeding have the highest risk for being life threatening. Traumatic injury to the chest can result in the loss of 25 percent of the body's BLOOD supply within minutes. A second- or third-degree burn that covers 36 percent of the body's surface results in extensive fluid and heat loss. Both circumstances cause rapid SHOCK. Though fractures are not as likely to be life threatening, an open FRACTURE exposes body tissues to high risk for INFECTION. As well, the BONE ends may sever blood vessels, resulting in hemorrhage.

These types of injuries present the highest risk of bloodborne infection, such as HEPATITIS and HIV/AIDS, for first responders. Latex or latex-type gloves are essential; the responder should be wearing them before touching the injured person. There is also the risk for injury to the responder, such as in a fire or explosion or when injuries result from VIOLENCE.

abrasions Scrape wounds that remove the outer layers of SKIN to expose the dermis and sometimes the subcutaneous layer beneath. Abrasions are common sports- and activity-related injuries resulting from falling or sliding on hard surfaces such as sidewalks, pavement, artificial turf, and hard-packed dirt.

Abrasions often look raw and may bleed; they usually hurt because they expose nerves and BLOOD vessels. Small abrasions are more nuisance than health problem. Large, deep abrasions may leave scars after they heal though most abrasions do not damage the dermis, the innermost layer of skin. Most abrasions require only minor first aid and heal uneventfully within two weeks.

These are the recommended steps for treating abrasions:

- Gently but thoroughly flush all dirt and debris from the abrasion with normal saline or a wound cleansing solution. Do not use soap and water or hydrogen peroxide; these formerly popular approaches delay scab formation and HEALING.
- Apply a topical antibiotic ointment and cover the abrasion completely with a bandage.
- Change the bandage daily or when it gets wet, applying fresh antibiotic ointment with each bandage change.
- Keep antibiotic ointment and a bandage on the abrasion until it heals, typically 7 to 10 days.

A health-care provider should assess and débride (clear away debris and damaged tissue) large abrasions to minimize the risk of scarring and INFECTION.

See also ANTIBIOTIC MEDICATIONS; LACERATIONS; SCAR.

avulsion An injury of force that tears away a body structure such as a TOOTH, segment of finger or toe, piece of tissue, or fragment of BONE. A major avulsion may involve a limb. Avulsion may be, though is not always, a type of TRAUMATIC AMPUTATION. Surgeons can replant some avulsed structures, such as teeth and bone fragments. The force that creates the separation often causes significant and irreparable damage to the tissues, however.

Site and situation assessment The responder should identify what caused the avulsion and if necessary neutralize its ability to do further damage. This includes turning off the power to any machinery or equipment that caused an avulsion injury.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens as nearly always there is moderate to heavy bleeding with avulsions.

First response actions Substantial bleeding is likely at the site of the avulsion. The first person to respond should take every practical effort to stop the bleeding. When possible, salvage the avulsed body part and protect it by wrapping it in sterile gauze moistened with sterile water or saline, if possible, and placing it in a plastic bag or container. Put the container in a portable cooler with ice around it and transport it to the hospital with the wounded person. Time is of the essence, however; the longer the avulsed part remains separated from the body the less likely the surgeon will be able to successfully replant it.

Follow-through An avulsion injury requires a physician's prompt evaluation and treatment, usually surgery either to replant the body part or surgically débride and repair the avulsion site.

See also BLEEDING CONTROL; BLOOD; PATHOGEN.

bleeding control The measures necessary to stop bleeding. Bleeding occurs when an injury damages the walls of the BLOOD vessels, allowing blood to escape.

Though profusely flowing blood may rapidly become life threatening, the amount of blood present or obvious is not always a good indication of the injury's severity. ABRASIONS (scrapes) and minor LACERATIONS (cuts) may appear to bleed extensively when they damage large numbers of the tiny blood vessels in the dermis (middle layer of the SKIN) and the subcutaneous layer, as these tissues contain a rich supply of blood. Wounds to the face and head tend to bleed especially profusely though often are not serious or life threatening. Injuries to the inside of the MOUTH not only bleed extensively but the blood also mixes with SALIVA, appearing as though there were even more blood. A nosebleed (EPISTAXIS) may also appear to produce a large amount of bleeding. However, the amount of blood lost with these types of injuries is usually minor.

BLOOD that spurts or surges from the wound comes from an ARTERY or major VEIN. Immediately apply pressure firmly enough to compress the blood vessel and maintain the pressure until emergency medical personnel take over.

Injuries that damage major veins or arteries can result in rapid loss of blood with risk for SHOCK and possible death. Bleeding in such circumstances is heavy and may spurt, gush, or surge from the injury. Life-threatening bleeding from the injury may also occur internally or as the result of BLUNT TRAUMA. Indications of INTERNAL BLEEDING include rapid swelling in the area of the bleeding and signs of shock in the injured person.

Site and situation assessment Situations of criminal VIOLENCE are often not safe for the first person who arrives to do any more than summon emergency aid. When injuries are due to animal bites, the responder must determine that the animal is no longer present or a threat. MOTOR VEHICLE ACCIDENTS may result in multiple injuries to the same person or to multiple people. Rapid SYMPTOM ASSESSMENT AND CARE TRIAGE is essential to determine whether any injuries appear life threatening.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens as well as to prevent BACTERIA on the responder's hands from causing INFECTION in the wound.

First response actions Bleeding frightens most people, those who are injured and those who are providing FIRST RESPONSE alike, especially when there appears to be a lot of blood. It is important for the responder to act calmly and comfortingly as well as quickly.

Use these measures to stop bleeding from an external injury such as an abrasion or laceration:

- Put on latex or latex-type gloves.
- Cover the injury with gauze bandages, a washcloth or towel, or even a wadded piece of clothing and apply firm, steady pressure.

- If the injury bleeds through the covering material, add more but do not remove the original covering.
- Maintain pressure until emergency medical personnel arrive.

Use these measures to stop a nosebleed:

- Put on latex or latex-type gloves.
- Have the person sit upright, holding the head tipped slightly toward the chest.
- Firmly squeeze both nostrils with the thumb and forefinger.
- Hold pressure in this way for at least 10 minutes.
- If bleeding starts again after releasing the pressure, repeat the procedure.

Follow-through A health-care provider should evaluate most bleeding injuries to cleanse them and determine whether sutures (stitches) or other treatments are necessary. Nosebleeds require medical attention when they persist or frequently recur.

See also GASTROINTESTINAL BLEEDING; IMPALEMENT; PUNCTURE WOUND; SYMPTOM ASSESSMENT AND CARE TRIAGE.

burns Injuries resulting from exposure to fire, intense heat, extremely hot water, electricity (including lightning), radiation (including ultraviolet radiation from sunlight or tanning systems), or caustic chemicals. The severity of a burn depends on the depth of penetration into the tissues (first degree, second degree, and third degree) and the amount of surface area the burn covers (percentage). SHOCK is a significant risk with any burn.

Medical personnel often use a method called the "rule of nines" to assess the body surface area a burn covers. This method assigns a percentage of 9 or 18 percent to regions of the body. For example, each arm is 9 percent, as is the head; the legs, back, and chest are each 18 percent. The surface area a burn covers may have more significant health consequences than the burn's depth. A first-degree (superficial) burn that covers an extensive area is often more serious than a third-degree burn that covers a very small area.

Heat and explosion burns on the upper body, face, and head may indicate the person also has burns to the MOUTH, NOSE, or upper airway (INHALATION BURNS). Such burns are potentially life threatening because swelling may close the airway, blocking the flow of oxygen to the LUNGS and compromising the ability to breathe.

Site and situation assessment Risk for injury to the first person to respond is very high when the source of the burn remains. In situations of active fire, risk for explosion, lightning, downed power lines, or chemical or radioactive contamination, the only response that may be safe for the responder is to provide as detailed information as possible when summoning emergency aid to help dispatchers send the appropriate equipment and trained personnel.

Responder personal protection measures Latex gloves, which the responder should put on before

BURN SEVERITY

Burn Classification	Extent of Burn	Symptoms
first degree or superficial thickness	burn penetrates only into the epidermis (outer layer of SKIN)	redness, PAIN, slight swelling
second degree or partial thickness	burn penetrates into the dermis (middle layer of skin)	blisters, pain, moderate swelling
third degree or full thickness	burn penetrates into the subcutaneous layer (innermost layer of skin) and possibly into underlying tissues	open wound or charring, may be no pain

approaching a person who has burns, are essential for personal protection from bloodborne pathogens as well as to prevent BACTERIA on the responder's hands from causing INFECTION in the burn wounds.

First response actions If the person's clothing is on fire, get the person on the ground and smother the flames by rolling or covering with a blanket, rug, jacket, or other object that can block the flow of air. Burns require specialized care from medical personnel trained in burn care. The most appropriate actions for an untrained responder first on the scene are to keep the person warm and comfort the person until medical personnel arrive. Most important:

- Do *not* put anything on the burns.
- Do *not* pull clothing or debris from the burns.
- Do *not* pop BLISTERS or pull the SKIN off blisters that spontaneously rupture.

Cool water, such as from a water faucet, is appropriate first aid to soothe small, minor burns. Promptly cooling a small first- or second-degree burn relieves PAIN and reduces swelling. However, the burn may still require medical attention.

Follow-through A health-care provider should evaluate and treat most second- and third-degree burns as well as first-degree burns that cover 36 percent or more of the body. Infection is a significant risk with second- and third-degree burns; any indications (FEVER, increased pain or swelling) require prompt medical assessment.

See also SITE AND SITUATION ASSESSMENT; SUNBURN; SYMPTOM ASSESSMENT AND CARE TRIAGE.

closed fracture A broken BONE that does not protrude through the surface of the SKIN. A closed FRACTURE most commonly results from a blow that delivers intense energy to small or limited area, causing the bone beneath to break. The bone ends may remain relatively aligned or may cause significant soft tissue damage even though the ends do not penetrate through the skin. Although the ends of the bones with a closed fracture do not break the skin, they may still do considerable damage to tissues and structures around the area of the break. Fractures require prompt evaluation and treatment from a health-care provider.

Do *not* move a person who may have a FRACTURE of the back or neck. Brace the person with rolled towels and blankets or other objects and keep him or her still until emergency medical personnel arrive.

The most appropriate action for the responder is to immobilize the limb, as well as the joints above and below the point of the fracture when possible, and obtain immediate medical attention. Splints are effective for fractures of the fingers, arms, and legs. Commercial first aid kits may include soft or inflatable splints. As well, the responder can use many common objects to fashion an improvised splint: towels, pillows, cardboard, and folded newspapers or magazines. A sling to support the arm on the side of the injury helps immobilize a fractured clavicle (collarbone) or shoulder blade (scapula). Scarves, belts, towels, and even a long-sleeve jacket or shirt with the sleeve pinned to the upper part of the garment are among the items the responder can use to make a sling.

See also ACCIDENTAL INJURIES; ATHLETIC INJURIES; OPEN FRACTURE; SYMPTOM ASSESSMENT AND CARE TRIAGE

dislocations Injury to the ligaments at a JOINT that allows the ends of the bones to separate. Often the responder cannot determine whether an injury is a dislocation or a CLOSED FRACTURE; FIRST RESPONSE treats them the same.

Do *not* attempt to "pop" a dislocated JOINT back into place.

The primary first response action is to immobilize the joint using a splint, or, in the case of a dislocated shoulder, a sling. A health-care provider should evaluate a dislocation to determine if there is a FRACTURE (which requires an X-RAY) and whether surgery is necessary to repair the ligaments.

See also ACCIDENTAL INJURIES; ATHLETIC INJURIES; BONE; LIGAMENT; SPRAINS AND STRAINS; SURGERY BENEFIT AND RISK ASSESSMENT.

impalement A wound in which an object penetrates a part of the body and remains embedded

there. Impalement injuries may occur when a person falls into a stationary object such as a fence rail or tree branch. Nail guns are responsible for numerous impalement injuries. Such injuries may penetrate a hand or foot in such a way as to nail it to a surface. Because nail guns expel nails under tremendous force, a nail may penetrate the skull or sternum to cause potentially life threatening injury. Impalement injuries may also occur when falling on an object such as a pencil.

Do *not* attempt to remove an impaled object from any part of the body. Immobilize the part as quickly as possible and summon emergency medical personnel.

Site and situation assessment Generally there are no risks to others at the site of an impalement injury. An exception might be in the circumstance of a nail gun, in which the responder must determine the nail gun is inactive.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens as there is often bleeding from an impalement injury.

First response actions It is crucial to avoid moving a person who is impaled on an immobile object and to provide as much information as possible about the object to the 911 dispatcher. The responder should stabilize the person to support the body or impaled body part and attempt to comfort and calm the person until emergency personnel arrive.

Follow-through Impalement injuries require a physician's assessment and medical treatment.

See also INFECTION; PUNCTURE WOUND; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE; TRAUMA TO THE EYE.

inhalation burns Thermal or chemical BURNS of the upper airway (TRACHEA) that result from BREATHING extreme heat (as in a fire) or toxic fumes. There may also be burns to the lips, tongue, and inside of the MOUTH and NOSE. Inhalation burns may cause rapid swelling of the airway, blocking the flow of air and presenting a life threatening situation. As emergency intubation or tracheotomy (invasive methods to bypass the upper airway to get air to the LUNGS) may be the only measures to save the person's life, the need for care from appropriate medical personnel is urgent.

Site and situation assessment The risk for injury to rescuers and others is high if there is still a burning or smoldering fire or a chemical exposure remains uncontained. A situation that requires personal protective equipment is one the first person to arrive should not enter.

Responder personal protection measures The responder should use a resuscitation shield if CARDIOPULMONARY RESUSCITATION (CPR) or RESCUE BREATHING is necessary.

First response actions Most inhalation burns are critical injuries that require advanced life support care well beyond the scope of untrained medical response. The most effective action on the part of the first person at the site is to rapidly summon emergency personnel.

Follow-through Inhalation burns require urgent medical treatment from physicians and other personnel trained and experienced in treating such injuries. Emergency transportation to a hospital or trauma center is often crucial.

See also ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS); INHALED TOXINS; SHOCK.

lacerations Cuts or tears of the skin and tissues. Lacerations may be fairly superficial or extend deep into the body. The risk for damage to nerves and BLOOD vessels is high. A large or deep laceration may bleed profusely, requiring immediate BLEEDING CONTROL efforts. A responder providing first aid for a laceration should put on latex or latex-type gloves approaching the injured person, are essential for personal protection from bloodborne pathogens as well as to prevent BACTERIA from the responder's hands from causing INFECTION in the wound.

To treat a mild laceration (less than ½ inch in length):

- Apply a bandage or gauze pad and hold it in place to stop any bleeding.
- When the bleeding stops, remove the bandage and apply an antibiotic ointment and a clean bandage.

- Change the bandage daily or when it gets wet, applying free antibiotic ointment with each bandage change.
- Continue to treat the laceration until its edges completely heal together (typically 7 to 10 days).

A laceration that is jagged or longer than ½ inch, or whose edges do not stay together, requires medical treatment. These are the recommended steps for the first responder to take to help protect the wound until the person can receive such treatment:

- Stop the bleeding; apply a bandage or other covering and hold it firmly enough to exert pressure.
- When the bleeding stops place gauze or tape to hold the bandage in place. Do *not* remove the bandage. If bleeding persists, add more bandage.
- Immobilize the area of the laceration to minimize and further damage.

Minor lacerations often heal well with self-treatment. When the edges of a laceration will not stay together on their own, the wound needs sutures (stitches). A jagged or deep laceration may require debridement, a procedure in which a doctor or physician's assistant numbs the area with a local anesthetic and trims away all loose tissue and cleans out any debris that contaminates the wound. The provider may suture the wound if it is clean enough or allow it to heal on its own, a process called granulation in which new tissue grows from the inside to the outside of the wound.

See also ABRASIONS; ANTIBIOTIC MEDICATIONS; AVULSION; SCAR.

open fracture A FRACTURE in which the broken BONE protrudes through the surface of the SKIN, creating an open wound that may bleed profusely. There is high risk for the bone ends to significantly damage nerves, BLOOD vessels, and other tissues in the area around the fracture.

Site and situation assessment Open fractures result from significant trauma as may occur in MOTOR VEHICLE ACCIDENTS, industrial accidents in which a heavy object falls on the person, falls, or collisions (such as when bicycling, skiing, or skateboarding). A person who has an open fracture may have multiple injuries or there may be multiple people involved in the accident who have various injuries. Possible site hazards that present risk of injury for responders, particularly the responder first to arrive, include downed power lines, unstable terrain or structures, and traffic.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens as nearly always there is moderate to heavy bleeding from open fractures.

First response actions Necessary actions from the first responder may include BLEEDING CONTROL, fracture stabilization, and comforting the injured person. Open fractures are serious injuries and moving the person is likely to require technical expertise as well as multiple rescuers. Often the most important role for the first responder is to keep the injured person calm, warm, and dry until rescue and emergency medical personnel arrive.

Follow-through Open fractures require urgent medical treatment and surgery to clean the injury and repair the fracture and damage to the surrounding tissues.

See also BODY SUBSTANCE ISOLATION; LACERATION; SHOCK; SYMPTOM ASSESSMENT AND CARE TRIAGE.

puncture wound An injury in which an object penetrates through the SKIN and into the underlying structures, sometimes deeply, with the wound closing with the object's withdrawal. There may be little or no external bleeding with a puncture wound. However, the risk for INFECTION is extremely high. First aid measures include rinsing debris and BLOOD from the wound and applying a bandage to protect it from exposure to further pathogens. A health-care provider should evaluate the wound promptly as it might be necessary to incise it (cut it open under sterile conditions) to clean it and irrigate it with antibiotic solution. The health-care provider is also likely to prescribe ANTIBIOTIC MEDICATIONS to treat bacterial INFECTION. The injured person should receive a tetanus toxoid booster if the last one was more than 10 years ago.

See also BODY SUBSTANCE ISOLATION; GUNSHOT WOUNDS; IMPALEMENT; NECROTIZING FASCIITIS; PATHOGEN; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE; TRAUMA TO THE EYE.

shock Life-threatening cardiovascular collapse. Shock occurs when BLOOD PRESSURE drops below the level necessary to pump BLOOD to the tissues (peripheral perfusion), depriving them of oxygen (HYPOXIA). The symptoms of shock may include

- clammy or bluish SKIN (CYANOSIS)
- confusion, anxiety, or disorientation
- diminished or loss of CONSCIOUSNESS
- rapid BREATHING (TACHYPNEA) and HEART RATE (tachycardia)
- difficulty BREATHING (DYSPNEA)

Urgent medical treatment is essential. While waiting for emergency medical personnel to arrive, the responder first on the scene should perform whatever emergency aid measures are appropriate for the person's circumstances. It is also important to keep the person warm and calm and to have the injured person lie as horizontally as is possible with the feet and legs elevated about 12 inches to help blood flow back to the HEART.

CIRCUMSTANCES THAT CAN RESULT IN SHOCK

ANAPHYLAXIS	BURNS
ELECTROCUTION	GUNSHOT WOUNDS
HEART ATTACK	HEAT STROKE
hemorrhage	MULTIPLE TRAUMA
OPEN FRACTURE	poisoning
severe DEHYDRATION	SPINAL CORD INJURY
TRAUMATIC AMPUTATION	TRAUMATIC BRAIN INJURY (TBI)

See also CARDIOPULMONARY RESUSCITATION (CPR); MULTIPLE TRAUMA; RESCUE BREATHING; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

soft tissue injuries Injuries to muscles, tendons, and ligaments that occur as a result of sudden excessive tension, causing the tissue to tear or stretch. Soft tissue injuries are common and may occur during everyday activities as well as during athletic activities. Soft tissue injuries tend to hurt and swell fairly immediately. Ice to the injured area is the most effective FIRST RESPONSE to reduce both PAIN and swelling. Immobilization, such as with elastic bandage wraps, splints, or slings, helps prevent further damage.

In general, a soft tissue injury requires evaluation and treatment from a doctor or other health-care provider when:

- the person cannot bear weight on a lower extremity or use an upper extremity
- swelling significantly distorts the appearance of the injured part
- over-the-counter (OTC) ANALGESIC MEDICATIONS such as acetaminophen or NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) fail to relieve pain

Though most soft tissue injuries are minor and heal with self-care measures in two to six weeks, severe injuries may require surgical repair, especially tears.

COMMON SOFT TISSUE INJURIES

ACHILLES TENDON INJURY	ANKLE INJURIES
groin pull	KNEE INJURIES
MUSCLE tears and pulls	SPRAINS AND STRAINS

See also ATHLETIC INJURIES; CLOSED FRACTURE; DISLOCATIONS; FRACTURE; HERNIA; INFLAMMATION; OPEN FRACTURE; SPRAINS AND STRAINS; SYMPTOM ASSESSMENT AND CARE TRIAGE.

Drowning

More than 4,000 Americans die from drowning each year. About 15,000 are revived and survive. The most common causes of drowning are swimming, boating, and scuba diving accidents. Though a person may struggle in the water for an extended time, the threshold for remaining submerged is only about three minutes, after which the BRAIN can no longer function and the person loses CONSCIOUSNESS.

When the head goes under the water a sequence of physiologic changes are activated, sometimes called the diving REFLEX, that alter the body's cardiovascular system to reserve BLOOD and the oxygen it carries to maintain the body's vital functions. The HEART RATE slows, BLOOD PRESSURE decreases, peripheral blood vessels constrict, blood supply to vital organs increases, and body temperature drops. These changes rapidly slow METABOLISM (the rate at which the body uses energy), significantly cutting the body's need for oxygen, which is one of the two fuel sources for cells (the other being GLUCOSE) throughout the body and the only fuel source for brain cells. When water enters the airway, the larynx severely spasms, closing off the TRACHEA. This laryngeal SPASM reflex is so intense that most people who die of drowning die from asphyxiation (lack of oxygen). In only about 10 percent of drownings does water enter the LUNGS.

The urge to save someone who is drowning is so strong that many would-be rescuers rush to jump into the water. However, water rescues are difficult. A person who is still struggling will often fight with the rescuer as a survival reaction, even to the extent of pushing the rescuer under the water. All too often the outcome is two drownings rather than a rescue. An unconscious drowning victim is easier to pull from the water, though nonetheless there is great risk for the rescuer who does not know water rescue techniques. Being a strong swimmer is not enough. Public pools, water parks, and swimming beaches typically have lifeguards and rescue equipment. Poles, rescue flotation rings, and other devices can allow a first responder to begin helping a drowning victim while waiting for trained rescue personnel to reach the scene.

cold water drowning Drowning that occurs when the water temperature is below 50°F. Survival is somewhat higher with cold water drowning because the cold temperature of the water seems to further depress METABOLISM, dramatically lowering the body's oxygen needs. Though in general a person who has been submerged in cold water for longer than 10 minutes has a poor chance for revival, some people have survived being under frigid water for 40 minutes. Rescue experts recommend initiating resuscitation efforts for all cold water drownings.

Site and situation assessment Important aspects of the situation include the type of water (pool, lake, river), how long the person has been under water, and whether other injuries are possible. SPINAL CORD INJURY or head injury is likely when diving into the water, for example.

Responder personal protection measures Essential responder personal protection items include latex or latex-style gloves and a resuscitation shield.

First response actions When the person is still in the water and is conscious, the responder should use items such as ropes, poles, and flotation devices to attempt to help the person rather than jumping into the water, unless the responder has training in water rescues. RESCUE BREATHING or CARDIOPUL-

MONARY RESUSCITATION (CPR) may be necessary when the person is brought to shore or the pool's edge.

Follow-through Emergency medical personnel typically transport cold water drowning victims to a hospital emergency department or trauma center even when resuscitative efforts appear unsuccessful because there is the possibility for revival when body temperature returns to normal. A doctor should thoroughly assess a person who survives, as secondary complications may occur.

See also RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE; WARM WATER DROWNING.

rescue breathing A method to revive a person who has stopped BREATHING (RESPIRATORY FAILURE) but who still has a HEART beat (PULSE). Rescue breathing may be necessary in drowning, poisoning, ELECTROCUTION, and other circumstances in which the respiratory failure occurs suddenly and the first response is rapid. The BRAIN begins to experience irreversible damage after about 6 minutes of oxygen deprivation, so urgent response is essential.

Site and situation assessment Risks for the first responder may include the continued presence of the cause of the person's respiratory failure, such as live electricity.

Responder personal protection measures Essential responder personal protection items include latex or latex-style gloves and a resuscitation shield.

First response actions Position the person to lie flat on his or her back and tilt the head back. Sometimes this action is sufficient to clear the airway and the person begins to breathe. Check for a PULSE (press two fingers against the side of the neck just beneath the notch at the back of the lower jaw) and watch and feel for signs of air movement. **When there is also no heart beat, CARDIOPULMONARY RESUSCITATION (CPR) is necessary.** CPR adds chest compressions to pump the heart to push BLOOD through the body. If there is a pulse but no evidence of air movement, begin rescue breathing:

1. Quickly look (and feel, if wearing latex gloves) inside the person's MOUTH for any objects that could block air from entering the airway (such as dentures, food, vomitus, or blood).
2. Place a resuscitation shield over the person's mouth, pinch the nostrils closed, and breathe with normal intensity into the shield (or the person's mouth) until the chest rises.
3. Give one breath about every five seconds. Pull away from the shield to allow air to leave the LUNGS.
4. Continue rescue breathing until the person resumes breathing independently or emergency medical personnel arrive and take over.

Follow-through A person who stops breathing requires urgent evaluation and treatment from a physician at a hospital emergency department or trauma center.

See also ANAPHYLAXIS; COLD WATER DROWNING; POISON PREVENTION; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE; WARM WATER DROWNING.

warm water drowning Drowning that occurs when the water temperature is higher than 60°F. Most warm water drownings take place in swimming pools and shallow lakes. The risk for death is very high when the person has been underwater longer than three minutes, thus rapid response is essential. However, there is great risk for the responder in an attempted rescue when the responder does not have training in water rescues.

Site and situation assessment Important aspects of the situation include the type of water (pool, lake, river), how long the person has been under water, and whether injuries in addition to drowning are possible. SPINAL CORD INJURY or head injury is likely when diving into the water, for example.

Responder personal protection measures Essential responder personal protection items include latex or latex-style gloves and a resuscitation shield.

First response actions When the person is still in the water and is conscious, the responder should use items such as ropes, poles, and flotation devices to attempt to help the person rather than jumping into the water, unless the responder

has training in water rescues. RESCUE BREATHING or CARDIOPULMONARY RESUSCITATION (CPR) may be necessary when the person is brought to shore or the pool's edge.

Follow-through Emergency medical personnel may decide whether to continue resuscitative efforts after they arrive and evaluate the situation. A physician should thoroughly assess a person who revives, as secondary complications may occur.

See also CARDIAC ARREST; COLD WATER DROWNING; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

Cardiac Arrest

Cardiac arrest—any circumstance in which the HEART stops beating—is immediately life-threatening. The BRAIN can survive only four to six minutes without oxygen, after which brain cells begin to die. Their loss is permanent. After 10 minutes without oxygen brain death occurs. The American Heart Association (AHA) identifies four actions, called the cardiac chain of survival, as crucial:

1. Call 911 to summon emergency medical aid.
2. Start CARDIOPULMONARY RESUSCITATION (CPR) to restore circulation.
3. Defibrillate (shock) the heart to restore functional electrical activity.
4. Get the person to a hospital for advanced cardiac life support care.

The first person to come upon a person who is in cardiac arrest sets this chain in motion and may perform the first two or three actions, depending on whether there is an AUTOMATED EXTERNAL DEFIBRILLATOR (AED) at the scene. The speed with which the first responder acts establishes the likelihood of survival. For optimal outcome, CPR must begin within four minutes of when the heart stops. A person who reaches step 4 within 30 minutes has the highest chance for survival.

COMMON CAUSES OF CARDIAC ARREST

ANAPHYLAXIS	ASPHYXIATION
diabetic SHOCK	drowning
ELECTROCUTION	HEART ATTACK
hemorrhage	MULTIPLE TRAUMA
poisoning	STROKE

cardiopulmonary resuscitation (CPR) Emergency efforts to restore the function of the HEART and circulation of BLOOD through the body. CPR combines RESCUE BREATHING with cardiac compressions. The first person to respond to a situation that requires CPR must first call 911 to summon emergency medical aid. Do not stop CPR once under way, unless the person begins to COUGH or breath independently or until trained medical personnel arrive to take over.

Essential responder personal protection items include latex or latex-style gloves and a resuscitation shield. To perform CPR:

1. Listen or feel for BREATHING and check for PULSE. If absent, continue with CPR.
2. Place the person on his or her back with the head tilted back.
3. Pinch closed the nostrils and open the MOUTH. Place the resuscitation shield and breathe into the shield (or the person's mouth) until the person's chest rises.
4. Place the palm of one hand on the back of the other hand and interlace the fingers.
5. Place the hands in the center of the person's chest. (For an infant under 12 months, use the flat of the fingers on the center of the chest between the nipples.)
6. Sharply push downward to compress the chest about 2 inches. Pump the person's chest in this way at the rate of 100 compressions per minute.
7. Give 2 normal breaths every 30 compressions.

When an AUTOMATED EXTERNAL DEFIBRILLATOR (AED) is available, a second responder may add DEFIBRILLATION to the resuscitation efforts, which is the next step. The AED unit determines whether defibrillation is appropriate.

See also COLD WATER DROWNING; RESCUE BREATHING; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE; WARM WATER DROWNING.

defibrillation Delivery of a controlled electrical shock, using an AUTOMATED EXTERNAL DEFIBRILLATOR (AED), to restore a functional HEART BEAT of a person who has suffered CARDIAC ARREST and whose HEART is in a state of fibrillation (rapid, disorganized, and useless contractions). Numerous public locations and businesses have AEDs.

The AED provides voice instruction for defibrillation. The AED pads, when placed on the person's chest as directed, first detect and send to the AED's computer the heart's electrical signals. If the rhythm is one that could respond to defibrillation, the AED prepares to deliver a preset electrical shock. If the heart is not beating or has a rhythm for which defibrillation is inappropriate the AED advises the responder what to do, which may be to perform CARDIOPULMONARY RESUSCITATION (CPR).

As with any life-threatening situation, the responder should first call 911 to summon emergency medical personnel.

See also HEART ATTACK; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SUDDEN CARDIAC DEATH; SYMPTOM ASSESSMENT AND CARE TRIAGE.

electrocution Injury resulting from electrical shock. Typically a person who experienced electrocution is not BREATHING and may not have a HEART beat, which is a life-threatening circumstance. The person is also likely to have electrical BURNS.

Do *not* approach a person who has suffered electrocution until certain the source of electricity is no longer active. Do *not* try to move a person who remains in contact with a high-voltage power line.

Site and situation assessment The scene of an electrocution is extremely hazardous. The first person to respond must determine whether the source of electricity remains "live." Indications of this include downed power lines and plugged in power tools or appliances. Water, including wet surfaces, increases the risk to the responder as water conducts electricity. There may also be risk for explosion or fire.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens. A resuscitation shield is necessary for personal protection when performing RESCUE BREATHING or full CARDIOPULMONARY RESUSCITATION (CPR).

First response actions When certain there is no live electricity at the scene, determine whether the person is breathing and has a heart beat. When necessary, begin rescue breathing or CPR. When these measures are not necessary, provide basic FIRST RESPONSE for burns and any other apparent injuries.

Follow-through The person requires urgent transportation to a trauma center or hospital emergency department. Burns are usually more severe than they appear and other injuries are likely.

See also PATHOGEN; RESPONDER SAFETY AND PERSONAL PROTECTION; SHOCK.

Heimlich maneuver A method to dislodge a foreign object from the upper airway that blocks the flow of air. The most common substances that become stuck and block BREATHING are incompletely chewed foods, especially meats, and small foods such as grapes, nuts, and hard candies. Young children may choke on nearly any food as well as small toys and other objects they pick up and put in their mouths.

To perform the Heimlich maneuver:

1. Confirm that the person is choking by asking him or her to speak. If the person cannot speak, the airway is blocked.
2. Stand behind the person, with the person standing.
3. Reach around the person and place one hand formed into a fist just above the person's belly button, thumb-side of the fist toward the person's body.

4. Grab the fist with the other hand and give a sharp pull inward and upward.
5. For an infant or small child, hold the infant in a sitting position. Use two or three fingers placed just above the belly button and jab sharply.
6. Repeat until the force of air pressure in the airway expels the object.

Rapid response is essential. Most people are fine once the object dislodges and they can breathe again. An object that does not come out with the Heimlich maneuver, or a person who loses CONSCIOUSNESS, requires further emergency care from trained medical personnel.

See also CARDIOPULMONARY RESUSCITATION (CPR); COUGH; RESCUE BREATHING; SWALLOWING DISORDERS.

Heat and Cold Injuries

Heat and cold injuries most often occur in response to environmental exposure to extremes in temperature. Environmental temperatures that are above or below the body's normal temperature require the body to implement actions to compensate. When the external temperature is higher than body temperature, these actions include peripheral vasodilation (BLOOD vessels in the extremities relax to increase the flow of blood), which moves greater quantities of blood closer to the body's surface where the temperature is somewhat cooler, and sweating, which cools the SKIN through evaporation.

When the external temperature is lower than body temperature, the body's compensatory mechanisms include peripheral vasoconstriction (blood vessels in the extremities narrow to decrease the flow of blood), which pulls more blood within the body core where temperature is somewhat warmer, and shivering, which increases energy output that in turn raises body temperature. When either set of mechanisms fails to achieve an acceptable body temperature, body chemistry and METABOLISM begin to change, altering vital body activities such as neurologic (BRAIN), cardiovascular (HEART rhythm and BLOOD PRESSURE), and renal (kidney) functions.

A person's body size and composition and activity level also influence the rate at which the body retains or loses heat. A person who has fairly high body fat loses body heat more slowly; he or she may have better tolerance for exposure to cold and less tolerance for exposure to heat. For a person who has low body fat, the reverse is the case: He or she often has better tolerance for exposure to heat and less for exposure to cold.

Moisture further influences the extent to which such exposure is tolerable or becomes a health concern. In cold water or when wearing wet clothing a person loses body heat at a rate up to 20 times that which occurs in cold air. Wind also influences the effects of cold; a calculation called the wind-chill factor represents the effect.

Moisture similarly affects the consequences of heat. High humidity in combination with high temperature intensifies the risk for heat injury; a calculation called the heat index represents the effect. HEAT EXHAUSTION and HEAT STROKE, the two types of heat-related injuries, most often occur in people who are engaged in intense physical activity in circumstances of combined high temperature and high humidity. DEHYDRATION can occur rapidly with heat injuries, further complicating health concerns.

Untreated, progressive heat or cold injury has high risk for permanent tissue and organ damage or death.

dehydration Insufficient water intake or excessive water loss resulting in electrolyte imbalance within the body. Though there are numerous possible causes for dehydration, the most common first aid scenario for dehydration occurs with athletic activities, sporting events, intense physical labor (especially in hot conditions), and extremely hot weather.

Early symptoms of dehydration include thirst, light-headedness, and dry SKIN. Drinking cool water, to 6 ounces every 15 minutes, is often adequate treatment for mild dehydration. Symptoms of moderate dehydration may include mild MUSCLE cramps, mental confusion, and disorientation. Though drinking water may improve moderate dehydration as a first aid response, intravenous fluids are often necessary to restore electrolyte balance. Severe dehydration may result in loss of CONSCIOUSNESS, rapid or irregular HEART RATE (tachycardia or ARRHYTHMIA), rapid BREATHING,

severe muscle cramps, and SHOCK. Severe dehydration requires urgent treatment from a hospital emergency department or trauma center.

COMMON CAUSES OF DEHYDRATION

acute GASTROENTERITIS	DIABETES
excessive diuretic use	excessive laxative use
heavy sweating	inadequate drinking
persistent DIARRHEA	persistent VOMITING
strenuous exercise	sustained FEVER

See also HEAT EXHAUSTION; HEAT STROKE.

heat exhaustion Overheating of the body in conditions of extreme heat or heavy physical activity. Symptoms of heat exhaustion come on suddenly and may include blanched SKIN, heavy sweating, NAUSEA, and lightheadedness. Get the person into a cool environment, such as a shaded area or an air-conditioned location, as quickly as possible. Loosen clothing, offer cool water or cool sports drinks (nothing iced), and spray or moisten the skin with cool water. When these measures are effective, the person improves dramatically and does not need further medical care.

Though heat exhaustion is mild and nearly always improves with appropriate interventions such as these, untreated heat exhaustion may progress to HEAT STROKE, a potentially life-threatening disturbance of body temperature. Call 911 to summon emergency medical aid if the person's temperature is higher than 102°F or the person has seizures.

See also DEHYDRATION; FEVER; SPORTS DRINKS AND FOODS.

heat stroke A life-threatening emergency in which the body is unable to lower body temperature. Heat stroke most commonly develops when there is a combination of intense physical activity and high environmental temperature. Though most people who develop heat stroke first experience HEAT EXHAUSTION, symptoms of heat stroke may appear suddenly. Such symptoms include

- hot, flushed SKIN
- absence of sweating
- HEADACHE
- rapid HEART RATE (tachycardia)
- HALLUCINATION
- disorientation, agitation, or loss of CONSCIOUSNESS
- seizures

Body temperature is usually above 102°F. Urgent treatment is necessary to avert permanent BRAIN and other neurologic damage. Call 911 to summon emergency medical aid, then get the person into an air-conditioned location, if possible, and remove outer layers of clothing. Spray a mist of water or apply cool, wet washcloths to the skin. If possible, place ice packs or extremely cold objects under the armpits and at the groin; at these locations large volumes of BLOOD circulate near the skin's surface. Position the person lying on his or her back with feet and legs elevated about 12 inches (SHOCK position). Emergency medical personnel may have cooling blankets and will begin intravenous fluids, then transport the person to a hospital or trauma center for further care.

See also DEHYDRATION; FEVER.

hypothermia The sustained loss of body heat resulting in low body temperature. Hypothermia occurs with extended exposure to cold external temperatures. Cool, wet conditions may also result in hypothermia. The key symptom of mild hypothermia, in which body temperature is no lower than 95°F, is intense shivering. Attempt to warm the person getting him or her into a warm location, removing wet clothing and wrapping in warm blankets, and offering warm fluids to drink.

When body temperature drops below 95°F in moderate hypothermia, the body loses the ability to shiver and the rate of heat loss increases. HEART RATE slows, BLOOD PRESSURE drops, and METABOLISM slows. The person is often confused or agitated, may paradoxically feel warm, and feels increasingly sleepy. Emergency response includes warming efforts as well as calling 911 to summon emergency aid personnel. Moderate hypothermia often requires further medical care to stabilize body temperature.

The lower body temperature drops, the less likely recovery becomes. Body temperature below 90°F, severe hypothermia, is very precarious.

Organ systems, especially the cardiovascular and neurologic, become exceedingly fragile. The risk for life-threatening ARRHYTHMIA (irregular heart beat) and especially VENTRICULAR FIBRILLATION is already high because of the body's altered metabolic and biochemical state; jostling the person during movement can rapidly destabilize the HEART and cardiovascular function. Severe hypothermia significantly slows neurologic function, causing UNCONSCIOUSNESS. The pupils are often fixed (nonresponsive to light). CARDIOPULMONARY RESUSCITATION (CPR) is necessary if the person is not BREATHING and has no PULSE. As with COLD WATER DROWNING, aggressive resuscitation efforts may revive someone who has had very low body temperature for an extended time.

See also FROSTBITE; HEAT EXHAUSTION; HEAT STROKE; RAYNAUD'S SYNDROME; SITE AND SITUATION ASSESSMENT.

Major Trauma

Major trauma is a circumstance of a single catastrophic injury, such as GUNSHOT WOUNDS or BURNS, or multiple injuries that affect multiple body systems in such a fashion that without urgent medical intervention death is likely. Major trauma most often results from events such as MOTOR VEHICLE ACCIDENTS, fires, serious falls, occupational accidents, and other situations in which the body encounters multiple hazards. Situations of major trauma are often more than an individual first responder can adequately assess. The top priority of FIRST RESPONSE is to get emergency personnel and equipment to the scene and prevent further injuries to the person or to others who are involved in the situation or arrive at the scene.

blunt trauma Injury that results from a strong blow or force. The injury may not be initially obvious because there may be no outward signs such as LACERATIONS or bruises. However, blunt trauma may cause internal bleeding or rupture of upper abdominal organs such as the SPLEEN or PANCREAS. Blunt trauma to the head may cause TRAUMATIC BRAIN INJURY (TBI).

Site and situation assessment MOTOR VEHICLE ACCIDENTS, industrial accidents, and collisions with stationary objects (such as a skier running into a tree) are among the situations that may result in multiple trauma.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from the possibility of acquiring INFECTION through contact with body fluids.

First response actions There are few FIRST RESPONSE measures for blunt trauma beyond keeping the injured person still and calm. SHOCK may be the only indication of internal bleeding from blunt trauma, which can be serious enough to cause rapid death. Surgery is the only means to treat internal bleeding.

Follow-through A health-care provider should evaluate blunt trauma to determine the need for further treatment.

See also CLOSED FRACTURE; SYMPTOM ASSESSMENT AND CARE TRIAGE; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

gunshot wounds Injuries that result from bullets. Gunshot wounds are often more serious than they appear, particularly when the bullet remains lodged in the body. A bullet enters the body with high velocity and follows a trajectory of least resistance. That trajectory may carry the bullet on a direct path through soft tissue or along the path of a BONE. Gunshot wounds may be accidental or intentional, self-inflicted or inflicted by another person.

Do *not* approach a person who has a gunshot wound or the site of a shooting if there is still gunfire or the whereabouts and status of the shooter are uncertain. Use extreme caution until the situation is clear.

Site and situation assessment The most essential determination is whether gunfire presents an ongoing risk for the injured person, other people, and responders.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens as nearly always there is moderate to heavy bleeding from gunshot injuries.

First response actions After calling 911 to summon emergency aid and then determining that

the situation is safe, try to locate the entrance and exit wounds. The entrance wound is often small and is easy to overlook, especially when the exit wound is large. BLEEDING CONTROL is critical; apply direct pressure to stop or slow bleeding. Do not move the injured person unless necessary for safety, as movement may cause further damage from a lodged bullet. SHOCK is likely; help the injured person to remain calm, warm, and as comfortable as possible.

Follow-through Gunshot wounds require urgent treatment at a hospital emergency department or trauma center.

See also MULTIPLE TRAUMA; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

head and spinal cord injuries Trauma that may cause BRAIN or neurologic damage. Common causes of head and SPINAL CORD injuries include collisions and accidents involving motor vehicles, motorcycles, bicycles, skiing, skateboarding, and diving into water. Indications of such injuries may include UNCONSCIOUSNESS, bleeding from the ears or NOSE, bruises around the eyes or behind the ears, HEADACHE, NAUSEA, and PARALYSIS.

Site and situation assessment Determine whether the injured person is at risk for further injury, such as from traffic or drowning. MOTOR VEHICLE ACCIDENTS may involve injuries to multiple people.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens as often there is moderate to heavy bleeding from traumatic injuries of the head and spinal cord.

First response actions Do *not* move a person who may have a head or SPINAL CORD INJURY. Use appropriate BLEEDING CONTROL when there are bleeding injuries. Head wounds especially can bleed profusely. To the best extent possible, brace or splint the person to immobilize the head and back. Discourage the person from attempting to move, including the arms and legs. Do *not* remove a helmet (bicycle, ski, motorcycle, football, horseback riding, or other type) unless the helmet interferes with aid attempts or the injured person's ability to breathe.

Follow-through Head injuries require urgent medical evaluation and treatment at a hospital emergency department or trauma center.

See also ACCIDENTAL INJURIES; CONCUSSION; TRAUMATIC BRAIN INJURY (TBI); SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

motor vehicle accidents Collisions between motor vehicles or between motor vehicles and objects. Accidental injuries are the fifth leading cause of death in the United States; motor vehicle accidents account for nearly half of those deaths. Nearly three million people receive injuries in motor vehicle accidents that require medical care. Motor vehicle accidents often result in multiple serious injuries affecting two or more people.

Site and situation assessment The situation the first person on the scene of an accident often encounters is chaotic and panicked. The responder must remain calm and clear headed to appropriately assess the circumstances and extent of injuries. Factors to consider include

- number of vehicles and people involved
- severity of injuries
- risks such as traffic, downed power lines, dangerous terrain (woods, cliffs, water), fire, leaking gasoline

Responder personal protection measures Latex gloves, which the responder should put on before approaching the scene, are essential for personal protection from bloodborne pathogens as nearly always there is moderate to heavy bleeding from injuries.

First response actions The responder often must act to concurrently provide a safer site and aid to those who have injuries. Sometimes the responder must help the injured out of the vehicles. The first actions of the responder include:

- Call 911 to summon rescue personnel.
- Turn off the ignitions of any vehicles that are still running.
- Kick dirt or gravel over any spilled gasoline to reduce risk for fire or explosion.
- Check for BREATHING; perform RESCUE BREATHING or CARDIOPULMONARY RESUSCITATION (CPR) when necessary.

- Stop bleeding.
- Speak calmingly and comfortingly to those involved in the accident.

Unless there is risk for fire or further injury, or it is necessary to remove the person from the vehicle to provide lifesaving first aid, it is usually best to wait for emergency personnel to safely evacuate or extricate people from their vehicles. Even injuries that appear mild may involve more serious damage that incorrectly moving the person could exacerbate.

Follow-through People who have moderate to severe injuries need further medical assessment and care. Medical aid personnel typically perform minimal treatment at the accident scene to stabilize the injured person's condition, with the goal of transporting the person to a hospital or trauma center within one hour of the accident. People who have mild injuries may desire to follow-up with their regular health-care providers.

See also BLEEDING CONTROL; BODY SUBSTANCE ISOLATION; CLOSED FRACTURE; MULTIPLE TRAUMA; OPEN FRACTURE; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

multiple trauma Numerous significant injuries such as may occur in MOTOR VEHICLE ACCIDENTS, shooting incidents, falls from high places, and fires. Multiple trauma is often life threatening and beyond the ability of the first responder to take much action beyond comforting the injured person until emergency medical personnel arrive.

Site and situation assessment Multiple trauma situations require rapid assessment of the nature and extent of the injuries, especially when numerous people are injured. The first person to respond to the scene of multiple trauma should also determine what risks are present that threaten responders and emergency personnel, such as unstable terrain, traffic, and crime scenes. Other important details include the number of people involved and the nature and seriousness of injuries.

Responder personal protection measures Latex gloves, which the responder should put on before approaching the scene or the injured person, are essential for personal protection from bloodborne pathogens as nearly always there is heavy bleeding with multiple trauma.

First response actions Multiple trauma is a difficult circumstance for an individual first responder to handle. After calling 911 to summon emergency personnel, priorities include checking the injured person's BREATHING and HEART beat, looking for bleeding, and providing basic first aid for SHOCK. CARDIOPULMONARY RESUSCITATION (CPR) and BLEEDING CONTROL may be necessary.

Follow-through A person who has multiple trauma is often gravely wounded and requires urgent medical care at a hospital emergency department or trauma center.

See also ACCIDENTAL INJURIES; BLEEDING CONTROL; BODY SUBSTANCE ISOLATION; BLUNT TRAUMA; GUNSHOT WOUNDS; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

trauma to the eye Penetrating or blunt force injuries to the EYE or the structures around the eye, flash BURNS, and chemical burns. Such injuries can cause partial or complete loss of vision as well as loss of the eye itself. Do only what is necessary to minimize movement and prevent further injury.

Do *not* remove an object that penetrates into the EYE, the eyelid, or the tissues around the eye.

For FIRST RESPONSE for eye trauma, cover the injured eye with a small paper cup or similar item to prevent contact with the eye or any object that might be penetrating the eye. Cover the uninjured eye with a bandage or cloth; covering both eyes prevents movement that could further damage the injured eye. Talk reassuringly and steadily to the person; being unable to see is disorienting and often frightening. Conversation helps the injured person maintain contact with his or her surroundings and know what is going on.

An ophthalmologist (physician who specializes in care of the eyes) should evaluate most eye injuries, even those that appear minor. Bacterial INFECTION in ABRASIONS and small LACERATIONS on the surface of the eye can threaten vision. Signifi-

cant injuries to the eye require urgent ophthalmologic care.

See also ACCIDENTAL INJURIES; BLACK EYE; CONJUNCTIVITIS; ENUCLEATION; IMPALEMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE; VISION IMPAIRMENT.

traumatic amputation The accidental or unintended severance of a body part. Fingers are the body parts most often lost to traumatic AMPUTATION. When the amputation is clean, such as may occur with a sharp object, surgeons may be able to reattach the amputated part. Avulsions (tearing of the structures) are often jagged and do considerable damage to the tissues, and the amputated part may not be intact enough to recover. Traumatic amputations typically bleed heavily and cause extreme PAIN. SHOCK is a significant risk.

Site and situation assessment It is important to salvage the amputated part and take it to the hospital with the injured person. A person who remains entangled in machinery remains at high risk for further injury unless properly extricated by emergency personnel trained in such situations. Power tools and appliances that remain plugged in create a hazard for further injury to the person or injury to the responder as well as the risk for ELECTROCUTION. The injured person may have MULTIPLE TRAUMA, depending on the cause of the traumatic amputation.

Responder personal protection measures Latex or latex-type gloves, which the responder should put on before approaching the injured person, are essential for personal protection from bloodborne pathogens as nearly always traumatic amputation results in heavy bleeding.

First response actions A major traumatic amputation is a difficult circumstance for an individual responder to handle. Call 911 to summon emergency medical aid, then attempt to control the bleeding. As with other bleeding injuries, direct pressure to the injury is the most effective method. Continue adding bandages, cloths, or other materials to establish bulk with the pressure. BLOOD loss may rapidly be substantial Try to keep the person warm and calm.

Follow-through Traumatic amputation typically requires emergency surgery to stop the bleeding, repair tissue damage, and reattach the amputated part when possible.

See also ACCIDENTAL INJURIES; AVULSION; BLEEDING CONTROL; BODY SUBSTANCE ISOLATION; MOTOR VEHICLE ACCIDENTS; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

Poisoning

Many substances are toxic when used inappropriately or through accidental exposure. Personal protection and safety are crucial for the first responder, who must first determine that there is no risk for becoming another victim of the same exposure. This is especially of concern with poisonous BITES AND STINGS, CONTACT TOXINS, and INHALED TOXINS. Though the FIRST RESPONSE should always be to call 911 to summon emergency medical aid, contact with a poison control telephone hotline can provide specific advice for the first responder until emergency medical personnel arrive. In the United States, there is a nationwide toll-free telephone hotline available 24 hours a day, 7 days a week.

US national poison control hotline:
1-800-222-1222
Available 24 hours a day, 7 days a week, from anywhere in the United States. The number is toll-free.

bites and stings Poisoning or HYPERSENSITIVITY RESPONSE (allergic reaction) to insect and reptile venoms. Though numerous insects sting and spiders and snakes bite, most are not poisonous (harmful beyond local discomfort at the site of the sting or bite). Rapid FIRST RESPONSE efforts can often reduce the severity of the resulting injury from poisonous stings and bites.

Remove rings, watches, and other jewelry in the area of a bite or sting to prevent further injury if swelling occurs. Significant swelling is especially common with poisonous snake bites.

Hymenoptera stings The most common stings come from wasps, hornets, yellow jackets, honey bees, and fire ants, collectively known as the Hymenoptera order. For the two million Americans who are allergic to the venom of these insects, the sting is far more significant than irritation or discomfort. Severe hypersensitivity response can cause swelling of the THROAT that blocks the airway; anaphylactic SHOCK is a life-threatening circumstance.

First response for Hymenoptera stings:

1. Gently scrape the stinger out of the wound with the edge of an object such as a credit card. Do *not* grasp the stinger with tweezers or fingernails as this squeezes the venom sack and forces more venom into the wound.
2. Apply ice until the area is numb.
3. Make a paste of baking soda and water and liberally spread it over the area of the sting. (Alternately, apply a small amount of hydrocortisone cream or diphenhydramine cream.)
4. Seek further evaluation and treatment from a health-care provider when PAIN persists or worsens, or when the person stung has a hypersensitivity response (allergic reaction).

Poisonous spider bites and scorpion stings There are only two types of poisonous spiders in North America, the widows (of which the black widow is the most notorious species) and the brown recluse. There is one species of poisonous scorpion, *Centruroides sculpturatus*, found in the southwestern United States (particularly Arizona) and northern Mexico. The venom of a widow spider is a neurotoxin that produces pain and swelling at the site of the bite and systemic effects that may include generalized discomfort or pain, MUSCLE CRAMP, and muscle SPASM. It may also elevate BLOOD PRESSURE (HYPERTENSION). Many people do not notice the bite of the brown recluse spider

for up to a week, when the toxin begins to cause tissue necrosis (death) at the site of the bite. The sting of the *C. sculpturatus* scorpion is also a neurotoxin; pain is immediate and later systemic response is common. Though unpleasant, these bites and stings are seldom fatal.

First response for poisonous scorpion stings and spider bites:

1. Apply ice to the bite.
2. Minimize movement of the bitten area; splint if possible.
3. Seek immediate medical care at a hospital emergency department. ANTIVENIN is available for widow spider and *C. sculpturatus* scorpion bites.

Poisonous snake bites There are four types of poisonous snakes in North America (see table), the bites of which are all capable of causing death. Antivenin is available for each type. Bites from poisonous snakes require urgent medical treatment at a hospital emergency department.

First response for snake bite:

1. Loosely splint or otherwise immobilize the area of the bite, and keep it lower than the HEART.
2. Keep the bitten person calm and still.
3. If it will be longer than 30 minutes before the bitten person can get to a hospital, wrap a bandage (or improvise with a scarf or other item of clothing) firmly but not tightly three to four inches above the bite, between the bite and the heart. The tightness of the wrap should be such that the responder's finger can fit under it. After placing such a bandage, do *not* remove it for any reason. Doing so will release a surge of venom into the person's BLOOD circulation.

Stings from stingrays, jellyfish, and sea urchins Numerous species common in the oceans in the coastal United States can deliver a significant sting. Stingrays and sea urchins sting with spines coated in venom. The spines may break off under the SKIN, continuing to release venom. They also present very high risk for bacterial INFECTION. Heat inactivates the venom and vinegar dissolves the spines. First response for stingray and sea urchin stings:

1. Soak the area of the sting in water as hot as the person stung can tolerate for at least 30 minutes.
2. After the hot water soak, place gauze pads soaked in vinegar over the sting area.
3. Repeat these measures until symptoms improve or the stung person reaches a hospital for further treatment.

Jellyfish and related creatures such as sea anemones and Portuguese man-o-war have clusters of long tentacles covered with stinging cells. First response for these stings:

1. Flush the area of the sting with seawater.
2. Place gauze pads soaked in vinegar over the sting area for at least 30 minutes.
3. Use gloved hands or tweezers to remove tentacles.
4. Repeat steps 2 and 3 until all tentacles are gone and pain subsides.
5. Seek treatment at a hospital emergency department.

See also ALLERGY; POISON PREVENTION.

contact toxins Substances, such as chemicals, that cause symptoms upon coming in contact with the SKIN. Many contact toxins cause mild symptoms such as contact DERMATITIS; some can cause chemical BURNS that require urgent or prompt medical care, depending on their severity. Rapid FIRST RESPONSE minimizes the severity of injury and prevents further absorption of the toxin through the skin and into the BLOOD circulation, if the toxin is one that absorbs in such of a way.

Site and situation assessment Determine the severity of symptoms and the toxin. When a chemical, take the container (with due caution to avoid contact with the ingredients) or label.

Responder personal protection measures Latex or latex-style gloves are essential to prevent responder contact with the toxin.

First response actions Call 911 to summon emergency medical personnel when situation appears significant or call the poison control hotline (in the United States: 1-800-222-1222) for guidance. Further first response actions:

POISONOUS SNAKES IN THE UNITED STATES

Type of Snake	Geographic Range	Characteristics of Bite
copperhead	much of United States from Texas to Rhode Island and the southern coast to the Ohio River valley	PAIN, swelling, and discoloration at the site of the bite that expand progressively systemic effects can cause significant illness bites of some species more toxic with risk of death treatment may require ANTIVENIN
coral snake	2 species in the US southeast, 1 species in the US southwest	venom is a powerful neurotoxin rapid systemic symptoms that may include NAUSEA, sleepiness, excessive drooling, difficulty BREATHING, and sometimes PARALYSIS high risk for death without prompt treatment antivenin need is urgent
cottonmouth, also called water moccasin	southern United States from eastern Texas to the northeast Maryland shore and inland to southern Missouri and western Tennessee	pain, swelling, and discoloration at the site of the bite that expand progressively systemic effects can cause significant illness bites of some species more toxic with risk of death treatment may require antivenin
rattlesnake	20 species diversely throughout United States and Mexico	pain, swelling, and discoloration at the site of the bite that expand progressively systemic effects can cause significant illness bites of some species more toxic with risk of death treatment may require antivenin

1. Remove any clothing contaminated by the toxin.
2. If the toxin is a dry powder, use gauze or a piece of fabric or a small brush to brush the powder off the skin.
3. After the powder is completely gone and for all other contact toxins, flush the area of contact (including the eyes if the toxin is in the eyes) with large amounts of water for at least 20 minutes. Hold or position the injured area such that the runoff water does not spread the toxin to other body parts or to the responder.

Follow-through Most poisonings resulting from contact poisons require further medical care to provide relief from symptoms such as itching, swelling, or PAIN. Chemical burns that form blisters (second-degree BURNS) or cover 10 percent or more of body surface require evaluation and treatment at a hospital emergency department or urgent care facility.

COMMON CONTACT TOXINS

ammonia	bleach
drain cleaners	gardening and yard products
household cleaning products	industrial solvents
lye	pesticides
poison ivy, oak, and sumac	stinging nettles

See also ACCIDENTAL INJURIES; POISON PREVENTION; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE; WORK AND OCCUPATIONAL SAFETY.

ingested toxins Substances, that when swallowed, can cause systemic poisoning. Ingestion may be intentional or accidental. Accidental ingestion of medications is the most common form of poisoning in children. Children may also eat or drink other substances not intended for consumption such as cleaning products, nail polish remover, and plants. Injury may range from gastrointestinal upset to life-threatening cardiovascu-

lar, kidney, LIVER, or neurologic damage. Appropriate FIRST RESPONSE is often crucial.

Site and situation assessment Determine, to the best extent possible, what and how much of it the person has swallowed, as well as when. Take the container or label when it is present.

Responder personal protection measures Latex or latex-style gloves are essential to prevent responder contact with the toxin as well as body fluids from the injured person. A resuscitation shield is necessary for RESCUE BREATHING or CARDIOPULMONARY RESUSCITATION (CPR).

First response actions Call 911 to summon emergency medical personnel when the situation appears significant or call the poison control hotline (in the United States: 1-800-222-1222) for guidance. Further first response actions:

1. If the person is conscious, give small, frequent drinks of water.
2. Do *not* give anything else and do *not* induce vomiting unless emergency medical or poison control personnel so instruct.
3. If the person is unconscious, position the person to lie on a side with the head somewhat down in case of VOMITING. If vomiting occurs, clear vomitus from the MOUTH to maintain an open airway.
4. If the person is not BREATHING, begin rescue breathing.
5. If the person is not breathing and does not have a PULSE, begin CPR.

Follow-through People who have ingested toxic substances or overdoses of medications require urgent treatment at a hospital emergency department or trauma center.

See also BODY SUBSTANCE ISOLATION; OVERDOSE; POISON PREVENTION; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SUICIDE IDEATION AND SUICIDE; SYMPTOM ASSESSMENT AND CARE TRIAGE.

inhaled toxins Substances that, when breathed, can injure the airways and LUNGS as well as cause systemic poisoning. Inhaled toxins require urgent medical care.

Site and situation assessment Attempt to determine the toxin and whether it remains present in the environment. There may be multiple

COMMON INHALED TOXINS

Toxin	Common Sources	Characteristics
carbon monoxide	poorly ventilated furnaces or stoves automobiles or gas power tools running in enclosed area such as garages	odorless symptoms include intense sleepiness progressing to loss of consciousness, bright redness to face
propane gas; natural gas	heating and cooking appliances	sulfuric odor ("rotten egg" smell) added to help detect leaks symptoms include disorientation and confusion progressing to loss of consciousness
ammonia gas	fertilizer products for commercial agricultural use industrial exposures	strong, pungent odor small exposure is highly toxic symptoms include severe respiratory irritation, intense coughing, and chemical BURNS to the nasal passages and airways
chlorine gas	pool cleaning products industrial exposures	strong, bleachlike odor symptoms include intense irritation to eyes, nose, and respiratory tract

people injured with environmental toxins such as chemical leaks.

Do *not* approach or enter an area where the possibility of environmental presence of the toxin exists.

Responder personal protection measures Latex or latex-style gloves are essential to prevent responder contact with the toxin as well as body fluids from the injured person. A resuscitation shield or mask is necessary for RESCUE BREATHING or CARDIOPULMONARY RESUSCITATION (CPR).

First response actions Call 911 to summon emergency medical personnel or call the poison control hotline (in the United States: 1-800-222-1222) for guidance. Many situations of inhaled toxins require self-contained BREATHING apparatus, protective clothing, and specialized training to safely rescue injured people. In such situations the first responder can only summon help. Do *not* perform rescue breathing or CPR without a resuscitation shield or mask, as doing so exposes the responder to the toxin.

Follow-through People exposed to inhaled toxins require urgent medical evaluation and treatment at a hospital emergency department or trauma center.

See also INHALATION BURNS; ORGANIC SOLVENTS; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

injected toxins Poisons that enter a person's body through injection with a needle subcutaneously (beneath the SKIN), intramuscularly (into a MUSCLE), or intravenously (into a VEIN). Most circumstances of injected toxins are inadvertent DRUG OVERDOSE resulting from ILLICIT DRUG USE. Illicit drugs may also contain poisons used as fillers or to dilute the drug.

Site and situation assessment Attempt to determine the drug or substance injected. Collect any vials, syringes, and other apparatus that may help identify the substance (handle these items only if wearing latex or latex-style gloves).

Responder personal protection measures Latex or latex-style gloves are essential to prevent responder contact with the toxin as well as body fluids from the injured person. A resuscitation shield or mask is necessary for RESCUE BREATHING or CARDIOPULMONARY RESUSCITATION (CPR). The risk for exposure to HEPATITIS, HIV/AIDS, and TUBERCULOSIS is very high when illicit drug abuse is the cause of the injected toxin poisoning.

First response actions Call 911 to summon emergency medical personnel and call the poison control hotline (in the United States: 1-800-222-1222) for guidance. Further first response actions:

1. If the person is conscious, try to keep him or her awake and moving.
2. If the person is unconscious, position the person to lie on a side with the head somewhat down in case of VOMITING. If vomiting occurs, clear vomitus from the MOUTH to maintain an open airway.
3. If the person is not BREATHING, begin rescue breathing using a resuscitation shield or mask.
4. If the person is not breathing and does not have a PULSE, begin CPR using a resuscitation shield or mask.

Follow-through Overdose or poisoning due to injected toxins requires urgent medical assessment and treatment at a hospital emergency department.

See also INJECTING DRUGS, RISKS OF; POISON PREVENTION; RESPONDER SAFETY AND PERSONAL PROTECTION; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

Radiation and Biochemical Injuries

Acts of terrorism using radiation, biologic pathogens, and chemical toxins became a heightened worldwide concern in the latter decades of the 20th century. Such acts have the potential to affect large numbers of people. Because the toxicity of these methods is very high, even FIRST RESPONSE requires a sophisticated public health approach. Injuries resulting from radiation, biologic, or chemical exposure may also occur through industrial accidents. RESPONDER SAFETY AND PERSONAL PROTECTION are crucial.

Radiation injuries Radiation injuries occur when there is exposure to radiation that exceeds the recommended safe limits. The exposure may be chronic (small exposure over time) or acute (sudden, massive exposure). Exposure to massive radiation doses results in acute radiation syndrome, which is often fatal. Radioactive substances that pose the greatest risk for radiation injuries include radionuclides, diethylenetriaminepentaacetate (DTPA), Neupogen, potassium iodide, and Prussian blue.

Biologic injuries Biologic injuries that occur when there is exposure to pathogens (BACTERIA and viruses) for which immunity is low are often serious or life-threatening illnesses. Among the pathogens of concern for intentional harm through biologic injury are those that cause ANTHRAX, BOTULISM, plague, and SMALLPOX.

Chemical injuries Chemical injuries that occur through intentional exposure to highly toxic chemicals, typically through inhalation or contact, often cause serious or fatal neurologic and pulmonary injury. Among the chemicals of concern are ammonia, arsenic, benzine, chlorine, cyanide, mercury, mustard gas, nitrogen mustard, osmium tetroxide, phosphine, ricin, sarin, tabun, thallium, and VX.

See also BODY SUBSTANCE ISOLATION; CHEMOTHERAPY; CONTACT TOXINS; ENVIRONMENTAL HAZARD EXPOSURE; HEAVY-METAL POISONING; INFECTION; INHALED TOXINS; PATHOGEN; POISON PREVENTION; RADIATION THERAPY; SITE AND SITUATION ASSESSMENT; SYMPTOM ASSESSMENT AND CARE TRIAGE.

APPENDIXES

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APPENDIX I
VITAL SIGNS

Vital signs are the observable, objective measures of a person's basic health status. The four standard vital signs are PULSE (HEART RATE), BLOOD PRESSURE, RESPIRATION RATE (BREATHING rate), and body temperature. Within a range of normal measurements, these signs vary among individuals and according to age, gender, aerobic condition, and level of physical activity. Health conditions further affect vital signs. A person may have vital signs that are outside the parameters of "normal" in a general context though are consistent for him or her.

VITAL SIGNS

	Heart Rate (Pulse)	Blood Pressure	Breathing Rate	Body Temperature
adult	60 to 89 beats per minute at rest	systolic < 120 millimeters of mercury (mm Hg) diastolic < 80 mm Hg	12 to 18 breaths per minute	97.8º to 99.1ºF
child, 1 to 8 years	80 to 100 beats per minute at rest	systolic <110 mm Hg	15 to 30 breaths per minute	97.8º to 99.1ºF
infant, 1 to 12 months	100 to 120 beats per minute at rest	systolic 70 to 100 mm Hg	25 to 50 breaths per minute	97.8º to 99.1ºF
infant, birth to 30 days	120 to 160 beats per minute at rest	systolic > 60 mm Hg	40 to 60 breaths per minute	97.8º to 99.1ºF

APPENDIX II
ADVANCE DIRECTIVES

Advance directives are instructions a person prepares that state his or her desires and preferences for end-of-life care. Typically advance directives consist of two legal documents

- a living will, which specifies the person's intentions in regard to medical treatment and resuscitative efforts
- a durable power of attorney for health care, also called durable medical power of attorney, which authorizes another individual (called a health-care agent or proxy) to make medical decisions on behalf of a person in the circumstance of a medical crisis when the person is unable to make such decisions

Advance directives are valid in all states in the United States, though each state has unique laws, regulations, and procedures for implementing advance directives. Documents should be updated, renewed, and resigned every few years to ensure currency. Information for obtaining and completing advance directive forms for each state is available through

National Hospice and Palliative Care Organization (NHPCO)
1700 Diagonal Road, Suite 625
Alexandria, VA 22314
703-837-1500
www.nhpco.org

APPENDIX III
GLOSSARY OF MEDICAL TERMS

afferent Moving inward or toward the body's center.

anastomosis A natural or surgically created connection between two structures.

arterial blood gases Measurement of the levels of oxygen (partial pressure of oxygen, Po_2) and carbon dioxide (partial pressure of carbon dioxide, Pco_2) in a sample of blood drawn from an artery. Tests may also measure the level of carbon monoxide and the blood's acidity (pH).

benign Harmless.

biopsy Removal of a tissue or fluid sample from the body to conduct pathologic examination for diagnostic purposes.

cabbage Pronunciation of the acronym "CABG," which stands for coronary artery bypass graft.

carcinogenic Capable of causing cancer.

complete blood count (CBC) Measure of the numbers and types (differentiation) of blood cells present in a sample drawn from a vein.

computed tomography (CT) scan A diagnostic imaging procedure that uses a computer to generate three-dimensional images from multiple, segmental X-rays. A CT scan may include ingestion or injection of a contrast medium to increase the density of structures, making them more visible via X-ray.

cyst An enclosed, saclike structure that may contain liquid or solid material.

dark adaptation test A test that assesses the ability to see in a dimly lighted environment.

deformity An abnormality of structure. Deformities, also called defects, may be congenital (present at birth) or acquired (result from injury or disease).

diagnosis The identification of a health condition, disorder, or disease.

diagnostic imaging Procedures that allow visualization of internal organs, structures, or processes to diagnose health conditions or monitor the progress of treatment. Common diagnostic imaging procedures include X-ray, ultrasound, computed tomography (CT) scan, and magnetic resonance imaging (MRI).

disease A health condition for which there are signs (objective and observable evidence) though the person may experience no symptoms (subjective perceptions).

donor A person who gives a structure or substance (blood, tissue, organ) to another person, the recipient.

dorsal The back, or spinal, surface.

efferent Moving outward or away from the body's center.

electrocautery The use of electrical current to generate heat capable of fusing bleeding blood vessels or eliminating tissue.

electromyography (EMG) A diagnostic procedure that uses electrodes attached to tiny needles inserted into selected muscles or placed on the surface of the skin, to measure the electrical activity in muscles to assess their function.

electronystagmography A diagnostic procedure that measures the electrical activity of the muscles that move the eyes.

fatigue Extended, persistent loss of physical, mental, and emotional energies and abilities.

fissure A natural division or channel in an organ or an abnormal split in a tissue.

fistula An abnormal opening between two structures.

fluoroscopy An imaging procedure that uses a steady stream of X-rays viewed on a monitor (television screen) to provide real-time, moving

images during diagnostic or therapeutic procedures such as cardiac catheterization.
fundus The base or body of a hollow organ.
graft Tissue, including whole organs, that a surgeon places within a person's body to treat a disease, defect, or deformity.
hematocrit A blood test to determine the percentage of red blood cells (erythrocytes) in a blood sample drawn from a vein.
hemorrhage Rapid and significant loss of blood.
home health care Medical providers such as nurses and physical therapists who provide treatment and care at the person's home.
hospice Care and support for a person who is terminally ill. Hospice providers may care for the person at home or in a hospice center.
humor Fluid within the body (from Latin, meaning "wet").
illness The perception of being unwell; the experience of symptoms.
in situ In the natural position or surroundings (in the body as opposed to in a test tube, for example).
in utero Contained within the uterus during pregnancy.
inferior Below or beneath.
integumentary A covering or cloak; refers to the skin.
ischemia Deprived of oxygen, usually as a consequence of restricted blood flow.
lap choly Medical shorthand for "laparoscopic cholecystectomy" (surgical removal of the gallbladder).
latent Delayed.
lateral Side.
lavage To rinse, wash, or flush with fluid.
lesion An abnormal growth of cells that are similar to, though altered from, the tissue from which they arise. Some injuries are also called lesions.
lifestyle Habits and practices in which a person chooses to engage that influence health and disease.
lobe A distinctive, defined section of an organ or gland.
localized Confined to a distinct area.
magnetic resonance imaging (MRI) A diagnostic imaging procedure that uses very powerful magnets to provide images of internal structures and organs. The MRI machine first emits a pulse of radiofrequency energy that causes the hydrogen atoms in the body to align in a uniform pattern. When the hydrogen atoms return to their normal alignment they send out electromagnetic signals that the MRI machine's magnets detect. A computer translates the signals into visual images.
malignant Capable of causing harm.
medically necessary A product, device, substance, or treatment that a person needs to recover from, accommodate to, or prevent injury or disease.
membrane A thin layer of tissue that covers or lines a structure or organ.
mucus A somewhat thick (viscous) fluid that glands or membranes produce.
occlusion Blockage.
organ A distinctive structure of tissues that performs a complex function within the body.
positron emission tomography (PET) scan A diagnostic imaging procedure that uses radionuclides, also called radioisotopes, to "see" cellular metabolism. The radionuclides (radioactive particles that rapidly disintegrate) enter cells attached to glucose molecules, which the cells use for energy. The rate at which the cells use the glucose, measured by tracking the rate of radionuclide disintegration, indicates whether the cells' function is normal; abnormal function may indicate disease such as cancer.
post After (in the context of time, as in postoperative).
primary Occurring without underlying cause.
prognosis The anticipated course of a health condition, disorder, or disease.
prone The position of lying with the chest and belly on the surface, with arms at the sides and legs outstretched.
recipient A person who receives a structure or substance (blood, tissue, organ) from another person, the donor.
resection The surgical removal of part of an organ or structure.
risk factor A circumstance that contributes to the likelihood for developing a disease.
Schirmer's test A procedure to assess the amount of tears the tear glands produce. The test involves placing tiny pieces of special paper at the edges of the eyelids, with the eyes closed, for five

minutes and then measuring the amount of fluid the paper absorbs.

scope of practice The legal, professional, and conventional responsibilities and duties of a health-care provider.

secondary Occurring as a consequence of another health condition, injury, disorder, disease, or treatment.

sensory perception Information the brain receives through the five senses: vision, hearing, smell, taste, and touch.

sign An objective observation of a body function or dysfunction.

single photon emission computed tomography (SPECT) scan A diagnostic imaging procedure that uses radionuclides to generate three-dimensional images of internal organs, structures, and functions. A special camera detects the presence of the radionuclides (rapidly disintegrating radioactive particles) in cells and tissues. Normal cells and tissues take up the radionuclides at known rates; unusual cell activity results in variations from these rates that may indicate health conditions such as infection or cancer.

speculum An instrument to hold apart the walls of an opening or hollow organ within the body to allow its examination.

spirometry A measure of the amount of air a person is capable of breathing in and breathing out, performed to assess basic pulmonary (lung) function.

standard of care The customary practices in diagnosis, treatment, and follow-up care as determined by professional health organizations.

superior Above.

supine The position of lying on the back with arms at the sides and legs outstretched.

suture A thread or wire used to hold closed the edges of a wound. Also called a stitch.

symptom A subjective perception of a body function or dysfunction.

syndrome A collection of symptoms, signs, and diagnostic findings that occurs in a particular pattern.

system Organs and structures of the body that work together to perform related, coordinated functions and activities.

teratogenic Capable of causing birth defects in a developing fetus.

tissue An organized group of cells that work collectively to perform a specific function.

transposition Body structures that are present but switched or exchanged in location or position; also called transposed.

tumor An abnormal growth of cells that are unique from the tissue from which they arise; also called a neoplasm.

ultrasound A diagnostic imaging procedure that uses focused sound waves to generate images of internal organs, structures, or functions. The sound waves reflect, or echo, from objects they encounter. A computer translates the echoes into electrical signals, which are displayed on a monitor screen as visual images.

vag hyst Medical short hand for "vaginal hysterectomy" (surgical removal of the uterus).

ventral The front, or belly, surface.

watchful waiting A planned treatment approach of observation and regular physician visits to monitor the status of a health condition.

APPENDIX IV
ABBREVIATIONS AND SYMBOLS

AA	Alcoholics Anonymous
ac	before eating (*ante cibum;* Latin)
ACTH	adrenocorticotropic hormone
ADH	antidiuretic hormone
ADHD	attention-deficit hyperactivity disorder
AED	automated external defibrillator
AFP	alpha-fetoprotein
AHA	alphahydroxy acid; American Heart Association
AIDS	acquired immunodeficiency syndrome
ALS	amyotrophic lateral sclerosis
AMC	arthrogryposis multiplex congenita
ANCA	antineutrophil cytoplasmic antibody
APLS	antiphospholipid syndrome
ARDS	adult respiratory distress syndrome
ARMD	age-related macular degeneration
ART	assisted reproductive technology
ASA	aspirin (acetylsalicylic acid)
ATC	certified athletic trainer
AuD	doctor of audiology
AV	atrioventricular
AVM	arteriovenous malformation
BALT	bronchus-associated lymphoid tissue
BCP	birth control pill
BID/bid	twice a day (*bis in die;* Latin)
BiPAP	bilevel positive airway pressure
BM	bowel movement
BMI	body mass index
BP	blood pressure
BPH	benign prostatic hyperplasia; benign prostatic hypertrophy
BPPV	benign paroxysmal positional vertigo
BSE	breast self-examination
BUN	blood urea nitrogen
$\overline{c}$	with (*cum;* Latin)
Ca	cancer
CABG	coronary artery bypass graft
CAD	coronary artery disease
CBC	complete blood count
cc	cubic centimeter
CDA	certified dental assistant
CDC	US Centers for Disease Control and Prevention
CEA	carcinoembryonic antigen
CICU	cardiac intensive care unit
CIN	cervical intraepithelial neoplasia
CIS	carcinoma in situ (cancer in the cell)
CJD	Creutzfeldt-Jakob disease
CLS/MT	clinical laboratory scientist/medical technologist
CMA	certified medical assistant
CMV	cytomegalovirus
CNM	certified nurse midwife
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
CP	cerebral palsy
CPAP	continuous positive airway pressure
CPhT	certified pharmacy technician
CPR	cardiopulmonary resuscitation
CRC	certified rehabilitation counselor
CRH	corticotropin-releasing hormone
CRNA	certified registered nurse anesthetist
CRNP	certified registered nurse practitioner
CRT	certified respiratory therapist
CSA	certified surgical assistant
CSF	cerebrospinal fluid; colony-stimulating factor
CST	certified surgical technologist
CST/CFA	certified surgical technologist/certified first assistant
CT	computed tomography
CTCL	cutaneous T-cell lymphoma
CTRS	certified therapeutic recreational specialist
CVD	cardiovascular disease

CVID	common variable immunodeficiency
CVS	chorionic villi sampling
D&C	dilation and curettage (also dilatation and curettage)
DASH	dietary approaches to stop hypertension
DC	doctor of chiropractic
DDS	doctor of dental surgery
DEA	US Drug Enforcement Agency
DES	diethylstilbestrol
DHEA	dehydroepiandrosterone
DIC	disseminated intravascular coagulation
dL (dl)	deciliter
DLE	discoid lupus erythematosus
DMARD	disease-modifying antirheumatic drug
DMD	doctor of dental medicine
DNA	deoxyribonucleic acid
DO	doctor of osteopathy
DRE	digital rectal examination
DrPH	doctor of public health
DTH	delayed-type hypersensitivity
DUB	dysfunctional uterine bleeding
DVT	deep vein thrombosis
EBCT	electron beam computed tomography
ECC	emergency cardiovascular care
ECG	electrocardiogram
ECT	electroconvulsive therapy
EECP	enhanced external counterpulsation
EEG	electroencephalogram
EENT	eyes, ears, nose, throat
EKG	electrocardiogram
EMG	electromyogram
EMT	emergency medical technician
EPO	erythropoietin
EPS	electrophysiology study
ERCP	endoscopic retrograde cholangiopancreatography
ESRD	end-stage renal disease
ESRF	end-stage renal failure
ESWL	extracorporeal shock wave lithotripsy
FAP	familial adenomatous polyposis
FDA	US Food and Drug Administration
FOBT	fecal occult blood test
FSH	follicle-stimulating hormone
GABA	gamma-aminobutyric acid
GAD	generalized anxiety disorder
GALT	gut-associated lymphoid tissue
GERD	gastroesophageal reflux disorder
GH	growth hormone
GHB	gamma hydroxybutyrate
GHRH	growth hormone–releasing hormone
GIFT	gamete intrafallopian transfer
GnRH	gonadotropin-releasing hormone
GPI	gastric inhibitive polypeptide
HAART	highly active antiretroviral therapy
Hg	mercury
HGE	human granulocytic ehrlichiosis
HHV	human herpesvirus
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HME	human monocytic ehrlichiosis
HNPCC	hereditary nonpolyposis colorectal cancer
HPV	human papillomavirus
HRT	hormone replacement therapy
IABP	intra-aortic balloon pump
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
ICD	implantable cardioverter defibrillator
ICSI	intracytoplasmic sperm injection
IgA	immunoglobulin A
IgD	immunoglobulin D
IgE	immunoglobulin E
IgG	immunoglobulin G
IgM	immunoglobulin M
IM	intramuscular
IND	investigational new drug
ITP	immune thrombocytopenic purpura
IUI	intrauterine artificial insemination
IV	intravenous
IVF	in vitro fertilization
IVP	intravenous pyelogram
L (l)	liter
LAAM	levo-alpha acetylmethadol
LAc	licensed acupuncturist
LAVH	laparoscopically assisted vaginal hysterectomy
LH	luteinizing hormone
LP	lumbar puncture
LPN	licensed practical nurse
LPT	licensed physical therapist
LQTS	long QT syndrome
LSD	lysergic acid diethylamide
LSW	licensed social worker
LVEF	left ventricular ejection fraction
LVN	licensed vocational nurse
m	meter

MAb (Mab)	monoclonal antibody
MAF	macrophage-activating factor
MALT	mucosa-associated lymphoid tissue
MD	doctor of medicine
MDMA	methylenedioxymethamphetamine
MEN	multiple endocrine neoplasia
MET	metabolic equivalent
MHC	major histocompatibility complex
MI	myocardial infarction
mL (ml)	milliliter
mm	millimeter
mm Hg	millimeters of mercury
MMR	measles/mumps/rubella (vaccine)
MRA	magnetic resonance angiography
MRI	magnetic resonance imaging
MS	multiple sclerosis
mtDNA	mitochondrial deoxyribonucleic acid
mtRNA	mitochondrial ribonucleic acid
NCCAM	National Center for Complementary and Alternative Medicine
ND	doctor of naturopathy
NDV	Newcastle disease virus
NIH	US National Institutes of Health
NK	natural killer
NPO	nothing by mouth (*non per os;* Latin)
NSAID	nonsteroidal anti-inflammatory drug
NTI	narrow therapeutic index
OC	oral contraceptives
OCD	obsessive–compulsive disorder
OCT	optical coherence tomography
OD	doctor of optometry
OMT	osteopathic manipulative treatment
OR	operating room
OTC	over the counter
OTR	registered occupational therapist
PA-C	certified physician assistant
PAT	paroxysmal atrial tachycardia
Pb	lead
pc	after eating (*post cibum;* Latin)
PCA	patient-controlled analgesia
PCID	partial combined immunodeficiency
PCOS	polycystic ovary syndrome
PCP	phencyclidine
PCTA	percutaneous transluminal coronary angioplasty
PDD	pervasive developmental disorder
PE	pulmonary embolism
PERP	positive end-respiratory pressure
PET	positron emission tomography
PharmD	doctor of pharmacy
PID	pelvic inflammatory disease
PKU	phenylketonuria
PMS	premenstrual syndrome
PNS	peripheral nervous system
PO	by mouth (*per os;* Latin)
POF	premature ovarian failure
PPI	proton pump inhibitor
PRN	as is needed (*pro re nata;* Latin)
PSA	prostate-specific antigen
PT-PTT	prothrombin time and partial thromboplastin time
PTA	physical therapy assistant
PTK	phototherapeutic keratectomy
PTSD	post-traumatic stress disorder
PUVA	psoralen and ultraviolet A
PVC	premature ventricular contraction
PVD	peripheral vascular disease
QD	once a day (*quaque die;* Latin)
QID	four times a day (*quartar in die;* Latin)
QN	once a night (*quaque noc;* Latin)
QOD	every other day (*quaque altera die;* Latin)
RA	rheumatoid arthritis
RBC	red blood count
RD	registered dietitian
RDH	registered dental hygienist
Rh	Rhesus (factor blood type)
RICE	rest, ice, compression, elevation
RN	registered nurse
RNA	ribonucleic acid
RPh	registered pharmacist
RRA	registered radiology assistant
RT	radiology technologist
s̄	without (*sans;* Latin)
SA	sinoatrial; surface area; surgeon's assistant
SAD	seasonal affective disorder
SALT	skin-associated lymphoid tissue
SAMe	S-adenosylmethionine
SARS	severe acute respiratory syndrome
SC	subcutaneous
SCI	spinal cord injury
SCID	severe combined immunodeficiency
SIDS	sudden infant death syndrome
sig	as instructed (*signa;* Latin)
SLE	systemic lupus erythematosus
SNP	single nucleotide polymorphism
SOB	shortness of breath

SPECT	single photon emission computed tomography
SPF	sun protection factor
SQ	subcutaneous
SSRI	selective serotonin reuptake inhibitor
STAT	immediately (*statim;* Latin)
STD	sexually transmitted disease
T_3	triiodothyronine
T_4	thyroxine
TBI	traumatic brain injury
TCA	trichloroacetic acid
TCM	traditional Chinese medicine
TENS	transcutaneous electrical nerve stimulation
TGF	transforming growth factor
TIA	transient ischemic attack
TID/tid	three times a day (*ter in die;* Latin)
TMLR	transmyocardial laser revascularization
TNF	tumor necrosis factor
TPMT	thiopurine methyltransferase
TRH	thyrotropin-releasing hormone
TSE	testicular self-examination
TSH	thyroid-stimulating hormone
TTP	thrombotic thrombocytopenic purpura
UA	urinalysis
URI	upper respiratory infection
URR	urea reduction ratio
USP	United States Pharmacopeia
UTI	urinary tract infection
UVA	ultraviolet A
UVB	ultraviolet B
VAD	ventricular assist device
VALT	vascular-associated lymphoid tissue
VBAC	vaginal birth after cesarean
vCJD	variant Creutzfeldt-Jakob disease
VIP	vasoactive intestinal peptide
WBC	white blood count
ZIFT	zygote intrafallopian transfer

APPENDIX V
MEDICAL SPECIALTIES AND ALLIED HEALTH FIELDS

MEDICAL PRACTITIONERS AND SPECIALTIES

Practitioner	Specialty	Practitioner	Specialty
anesthesiologist	anesthesiology; anesthesia during surgery, pain management	neonatologist	neonatology; newborns
		nephrologist	nephrology; kidney conditions
bariatrician	bariatrics; obesity	neurologist	neurology; nervous system
cardiologist	cardiology; heart and blood vessels	obstetrician	obstetrics; pregnancy and childbirth
chiropractor	chiropractic; spine and back	oncologist	oncology; cancer
dermatologist	dermatology; integumentary system (skin, hair, nails)	ophthalmologist	ophthalmology; eyes
		optometrist	optometry; vision correction
endocrinologist	endocrinology; endocrine glands	orthopedist	orthopedics; musculoskeletal system
epidemiologist	epidemiology; trends in health and disease	otolaryngologist	otolaryngology; ear, nose and throat
		pathologist	pathology; tissue examination
family practitioner	family practice; medical and surgical care, children and adults	pediatrician	pediatrics; children (birth through adolescence)
gastroenterologist	gastroenterology; gastrointestinal system	physiatrist	physiatry; physical and rehabilitative medicine
geneticist	genetics; inherited and metabolic diseases	podiatrist	podiatry; feet
		psychiatrist	psychiatry; mental disorders
geriatrician	geriatrics; elderly	psychologist	mental health counseling
gynecologist	gynecology; women's reproductive system	pulmonologist	pulmonology; lungs
		radiologist	radiology; diagnostic and therapeutic radiologic and nuclear medicine procedures
hematologist	hematology; blood and circulation		
hospitalist	care for hospitalized patients		
immunologist	immunology; immune system conditions and allergies	rheumatologist	rheumatology; rheumatic diseases
		surgeon	surgery; surgical operations
internist	internal medicine; adult health care (except surgery)	urologist	urology; urologic system, male reproductive system

APPENDIX VI
RESOURCES

The resources cited in this section offer up-to-date treatment and research information. Most have access through written communication, telephone, and Web sites. As Internet access becomes more available, many organizations find the World Wide Web to be the most efficient means for providing current and varied information. Consequently, some organizations are shifting their point of contact entirely to their Web sites. Though the contact information for these resources is current at the time of *The Facts On File Encyclopedia of Health and Medicine's* publication, it is subject to change. For additional resource material, please see the section "Bibliography and Further Reading."

GENERAL

Administration for Children and Families (ACF)
US Department of Health and Human Services (HHS)
370 L'Enfant Promenade SW
Washington, DC 20447
www.acf.hhs.gov

Administration on Aging (AoA)
US Department of Health and Human Services (HHS)
Washington, DC 20201
202-619-0724
www.aoa.gov

Agency for Healthcare Research and Quality (AHRQ)
US Department of Health and Human Services (HHS)
Office of Communications and Knowledge Transfer
540 Gaither Road, Suite 2000
Rockville, MD 20850
www.ahcpr.gov

American Academy of Family Physicians (AAFP)
PO Box 11210
Shawnee Mission, KS 66207-1210
913-906-6000 / 800-274-2237
www.aafp.org

American Academy of Pediatrics (AAP)
141 Northwest Point Boulevard
Elk Grove Village, IL 60007-1098
847-434-4000
www.aap.org

American Board of Medical Specialties (ABMS)
1007 Church Street, Suite 404
Evanston, IL 60201-5913
847-491-9091
www.abms.org

American Medical Association
515 North State Street
Chicago, IL 60610
800-621-8335
www.ama-assn.org

Centers for Medicare & Medicaid Services (CMS)
US Department of Health and Human Services (HHS)
7500 Security Boulevard
Baltimore, MD 21244
800-MEDICARE (800-633-4227)
TTY: 877-486-2048
www.cms.hhs.gov

ClinicalTrials.gov
US National Institutes of Health (NIH)
www.clinicaltrials.gov

Health Resources and Services Administration (HRSA)
US Department of Health and Human Services (HHS)
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857
www.hrsa.gov

Indian Health Service (IHS)
US Department of Health and Human Services
The Reyes Building
801 Thompson Avenue, Suite 400
Rockville, MD 20852
www.ihs.gov

National Center for Health Statistics (NCHS)
US Centers for Disease Control and Prevention (CDC)
3311 Toledo Road
Hyattsville, MD 20882
301-458-4000 / 866-441-NCHS (866-441-6247)
www.cdc.gov/nchs/

National Center on Minority Health and Health Disparities (NCMHD)
US National Institutes of Health (NIH)
6707 Democracy Boulevard, Suite 800, MSC 5465
Bethesda, MD 20892-5465
301-402-1366
TTY: 301-451-9532
www.ncmhd.nih.gov

National Institute on Aging (NIA)
US National Institutes of Health (NIH)
Building 31, Room 5C27
31 Center Drive, MSC 2292
Bethesda, MD 20892
301-496-1752
TTY: 800-222-4225
www.nia.nih.gov

National Library of Medicine (NLM)
US National Institutes of Health (NIH)
8600 Rockville Pike
Bethesda, MD 20894
301-594-5983 / 888-346-3656
www.nlm.nih.gov

National Organization for Rare Disorders (NORD)
55 Kenosia Avenue, PO Box 1968
Danbury, CT 06813-1968
203-744-0100
TDD: 203-797-9590
www.rarediseases.org

Office of the Surgeon General
US Department of Health and Human Services (HHS)
5600 Fishers Lane, Room 18066
Rockville, MD 20857
301-443-4000
www.surgeongeneral.gov

Office on Women's Health
US Department of Health and Human Services (HHS)
200 Independence Avenue SW, Room 712E
Washington, DC 20201
202-690-7650
www.womenshealth.gov

US Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201
202-619-0257 / 877-696-6775
www.hhs.gov

US Food and Drug Administration (FDA)
5600 Fishers Lane
Rockville, MD 20857-0001
888-INFO-FDA (888-463-6332)
www.fda.gov

US National Institute of Environmental Health Sciences (NIEHS)
PO Box 12233
Research Triangle Park, NC 27709
919-541-3345
www.niehs.nih.gov

US National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, MD 20892
301-496-4000
TTY: 301-402-9612
www.nih.gov

US Social Security Administration (SSA)
Office of Public Inquiries
Windsor Park Building
6401 Security Boulevard
Baltimore, MD 21235
800-772-1213
www.ssa.gov

VOLUME 1

The Ear, Nose, Mouth, and Throat

Alexander Graham Bell Association for the Deaf and Hard of Hearing (AG Bell)
3417 Volta Place NW
Washington, DC 20007-2778
202-337-5220 / 866-337-5220
TTY: 202-337-5221
www.agbell.org

American Society for Deaf Children (ASDC)
PO Box 3355
Gettysburg, PA 17325
717-334-7922 / 800-942-ASDC (800-942-2732)
www.deafchildren.org

American Speech-Language-Hearing Association (ASHA)
10801 Rockville Pike
Rockville, MD 20852
301-897-5700 / 800-638-8255
TTY: 301-897-0157
www.asha.org

National Association of the Deaf (NAD)
814 Thayer Avenue, Suite 250
Silver Spring, MD 20910-4500
301-587-1788
TTY: 301-587-1789
www.nad.org

National Institute on Deafness and Other Communication Disorders (NIDCD)
US National Institutes of Health (NIH)
31 Center Drive, MSC 2320
Bethesda, MD 20892-2320
800-241-1044
TTY: 800-241-1055
www.nidcd.nih.gov

The Eyes

American Academy of Ophthalmology
PO Box 7424
San Francisco, CA 94120
415-561-8500
www.aao.org

American Optometric Association
243 North Lindbergh Boulevard
St. Louis, MO 63141
314-991-4100
www.aoanet.org

American Society of Ophthalmic Plastic and Reconstructive Surgery
1133 West Morse Boulevard, #201
Winter Park, FL 32789
407-647-8839
www.asoprs.org

Lighthouse International
111 East 59th Street
New York, NY 10022-1202
800-829-0500
www.lighthouse.org

National Eye Institute (NEI)
US Institutes of Health (NIH)
2020 Vision Place
Bethesda, MD 20892-3655
301-496-5248
www.nei.nih.gov

Prevent Blindness America
500 East Remington Road
Schaumburg, IL 60173
847-843-2020 / 800-331-2020
www.preventblindness.org

The Integumentary System

American Society for Dermatologic Surgery
5550 Meadowbrook Drive, Suite 120
Rolling Meadows, IL 60008
847-956-0900
asds-net.org

International Pemphigus Foundation
The Atrium Plaza, Suite 210
828 San Pablo Avenue
Albany, CA 94706
510-527-4970
www.pemphigus.org

National Organization for Albinism and Hypopigmentation (NOAH)
PO Box 959
East Hampstead, NH 03826-0959
603-887-2310 / 800-473-2310
www.albinism.org

National Pediculosis Association, Inc.
50 Kearney Road
Needham, MA 02494
781-449-NITS (781-449-6487)
www.headlice.org

National Psoriasis Foundation
6600 Southwest 92nd Avenue, Suite 300
Portland, OR 97223-7195
503-244-7404 / 800-723-9166
www.psoriasis.org

The Nervous System

Alzheimer's Disease Education & Referral Center (ADEAR)
PO Box 8250
Silver Spring, MD 20907-8250
800-438-4380
www.alzheimers.org

American Academy of Neurology
1080 Montreal Avenue
St. Paul, MN 55116
651-695-2717 / 800-879-1960

American Parkinson Disease Association
135 Parkinson Avenue
Staten Island, NY 10305
718-981-8001 / 800-223-2732
www.apdaparkinson.org

Huntington's Disease Society of America
505 Eighth Avenue, Suite 902
New York, NY 10018
212-242-1968 / 800-345-HDSA (800-345-4372)
www.hdsa.org

International Dyslexia Association
8600 LaSalle Road
Chester Building, Suite 382
Baltimore, MD 21286-2044
410-296-0232 / 800-ABCD123 (800-222-3123)
www.interdys.org

Learning Disabilities Association of America
4156 Library Road, Suite 1
Pittsburgh, PA 15234-1349
412-341-1515
www.ldaamerica.org

Michael J. Fox Foundation for Parkinson's Research
Grand Central Station
PO Box 4777
New York, NY 10163
800-708-7644
www.michaeljfox.org

Multiple Sclerosis Association of America (MSAA)
706 Haddonfield Road
Cherry Hill, NJ 08002
856-488-4500
www.msaa.com

National Center for Learning Disabilities
381 Park Avenue South, Suite 1401
New York, NY 10016
212-545-7510 / 888-575-7373
www.ld.org

National Institute of Neurological Disorders and Stroke (NINDS)
US Institutes of Health (NIH)
PO Box 5801
Bethesda, MD 20824
301-496-5751 / 800-352-9425
TTY: 301-468-5981
www.ninds.nih.gov

National Multiple Sclerosis Society
733 Third Avenue
New York, NY 10017
800-FIGHT-MS (800-344-4867)
www.nationalmssociety.org

National Parkinson Foundation
1501 Northwest 9th Avenue/Bob Hope Road
Miami, FL 33136-1494
00-327-4545
www.parkinson.org

Parkinson's Disease Foundation
1359 Broadway, Suite 1509
New York, NY 10018
212-923-4700 / 800-457-6676
www.pdf.org

United Cerebral Palsy
1660 L Street NW, Suite 700
Washington, DC 20036
202-776-0406 / 800-872-5827
TTY: 202-973-7197
www.ucp.org

The Musculoskeletal System

American Association of Orthopaedic Surgeons (AAOS)
6300 North River Road
Rosemont, IL 60018-4262
847-823-7186 / 800-346-AAOS (800-346-2267)
www.aaos.org

Arthritis Foundation
1330 West Peachtree Street, Suite 100
Atlanta, GA 30309
404-872-7100
800-568-4045
www.arthritis.org

Muscular Dystrophy Association (MDA)
3300 East Sunrise Drive
Tucson, AZ 85718
800-FIGHT-MD (800-344-4863)
www.mdausa.org

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Information Clearinghouse
US National Institutes of Health (NIH)
1 AMS Circle
Bethesda, MD 20892-3675
301-495-4484 / 877-226-4267
TTY: 301-565-2966
www.niams.nih.gov

National Institute of Dental and Craniofacial Research (NIDCR)
US National Institutes of Health (NIH)
45 Center Drive, Room 4AS19, MSC 6400
Bethesda, MD 20892-6400
301-496-4261
www.nidcr.nih.gov

National Osteoporosis Foundation
1232 Twenty-second Street NW
Washington, DC 20037-1292
202-223-2226
www.nof.org

Pain and Pain Management

American Chronic Pain Association (ACPA)
PO Box 850
Rocklin, CA 95677-0850
916-632-0922 / 800-533-3231
www.theacpa.org

American Council for Headache Education
19 Mantua Road
Mt. Royal, NJ 08061
856-423-0258 / 800-255-ACHE (800-255-2243)
www.achenet.org

American Pain Foundation
201 North Charles Street
Suite 710
Baltimore, MD 21201
888-615-PAIN (888-615-7246)
www.painfoundation.org

National Chronic Pain Outreach Association (NCPOA)
PO Box 274
Millboro, VA 24460
540-862-9437
www.chronicpain.org

National Foundation for the Treatment of Pain
PO Box 70045
Houston, TX 77270
713-862-9332
www.paincare.org

National Headache Foundation
820 North Orleans, Suite 217
Chicago, IL 60610-3132
773-388-6399 / 888-NHF-5552 (888-643-5552)
www.headaches.org

VOLUME 2

The Cardiovascular System

American College of Cardiology
Heart House
9111 Old Georgetown Road
Bethesda, MD 20814-1699
301-897-5400 / 800-253-4636, ext. 694
www.acc.org

American Heart Association
7272 Greenville Center
Dallas, TX 75231
800-AHA-USA1 (800-242-8721)
www.americanheart.org

American Stroke Association
7272 Greenville Avenue
Dallas, TX 75231
888-4STROKE (888-478-7653)
www.strokeassociation.org

The Mended Hearts, Inc.
7272 Greenville Avenue
Dallas TX 75321
214-706-1442 / 888-HEART99 (888-432-7899)
www.mendedhearts.org

The Blood and Lymph

American Association of Blood Banks (AABB)
8101 Glenbrook Road
Bethesda, MD 20814-2749
301-907-6977
www.aabb.org

National Heart, Lung, and Blood Institute (NHLBI) Health Information Center
National Institutes of Health
PO Box 30105
Bethesda, MD 20824-0105
301-592-8573
www.nhlbi.nih.gov

The Pulmonary System

American Lung Association/American Thoracic Society
1740 Broadway
New York, NY 10019-4374
800-LUNG-USA
www.lungusa.org

The Immune System and Allergies

Allergy and Asthma Network/Mothers of Asthmatics, Inc.
3554 Chain Bridge Road, Suite 2000
Fairfax, VA 22030
800-878-4403
www.podi.com/health/aanma

American Academy of Allergy, Asthma and Immunology
611 East Wells Street
Milwaukee, WI 53202
800-822-ASMA
www.aaaai.org

American College of Allergy, Asthma and Immunology
85 West Algonquin Road, Suite 550
Arlington Heights, IL 60005
800-842-7777
www.allergy.mcg.edu

American College of Rheumatology
1800 Century Place, Suite 250
Atlanta, GA 30345
404-633-3777
www.rheumatology.org

Asthma and Allergy Foundation of America
1125 Fifteenth Street NW, Suite 502
Washington, DC 20036
202-466-7643 / 800-7ASTHMA
www.aafa.org

Food Allergy and Anaphylaxis Network
10400 Eaton Place, Suite 107
Fairfax, VA 22030
800-929-4040
www.foodallergy.org

JAMA Asthma Information Center
American Medical Association
515 North State Street
Chicago, IL 60610
www.ama-assn.org/asthma

Lupus Foundation of America, Inc.
2000 L Street NW, Suite 710
Washington, DC 20036
202-349-1155 / 800-558-0121
www.lupus.org

Parents of Asthmatic/Allergic Children
1412 Marathon Drive
Ft. Collins, CO 80524
303-842-7395

Scleroderma Foundation
12 Kent Way, Suite 101
Byfield, MA 01922
800-722-4673
www.scleroderma.org

Sjögren's Syndrome Foundation
366 North Broadway
Jericho, NY 11753
516-933-6365 / 800-475-6473
www.sjogrens.org

Infectious Diseases

National Institute of Allergy and Infectious Diseases (NIAID)
US National Institutes of Health
Bethesda, MD 20892
www.niaid.nih.gov

Cancer

American Cancer Society (ACS)
1599 Clifton Road NE
Atlanta, GA 30329
800-ACS.2345 (800-227-2345)
www.cancer.org

National Cancer Institute (NCI)
US National Institutes of Health (NIH)
NCI Public Inquiries Office
6116 Executive Boulevard, Room 3036A
Bethesda, MD 20892-8322
800-4-CANCER (800-422-6237)
www.cancer.gov

National Comprehensive Cancer Network (NCCN)
500 Old York Road, Suite 250
Jenkintown, PA 19046
215-690-0300 / 888-909-NCCN (888-909-6226)
www.nccn.org

VOLUME 3

The Gastrointestinal System

American College of Gastroenterology (ACG)
PO Box 342260
Bethesda, MD 20827-2260
301-263-9000
www.acg.gi.org

American Gastroenterological Association (AGA)
4930 Del Ray Avenue
Bethesda, MD 20814
301-654-2055
www.gastro.org

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
US National Institutes of Health (NIH)
Office of Communications and Public Liaison
Building 31, Room 9A04
31 Center Drive, MSC 2560
Bethesda, MD 20892-2560
www.niddk.nih.gov

The Endocrine System

American Diabetes Association
National Call Center
1701 North Beauregard Street
Alexandria, VA 22311
800-DIABETES (800-342-2383)
www.diabetes.org

American Thyroid Association
6066 Leesburg Pike, Suite 500
Falls Church, VA 22041
703-998-8890 / 800-THYROID (800-849-7643)
www.thyroid.org

National Diabetes Education Program
One Diabetes Way
Bethesda, MD 20814-9692
301-496-3583
www.ndep.nih.gov

The Urinary System

National Kidney Foundation
30 East 33rd Street
New York NY 10016
800-622-9010
www.kidney.org

The Reproductive System

Alan Guttmacher Institute (AGI)
120 Wall Street, 21st Floor
New York, NY 10005
212-248-1111
800-355-0244
www.agi-usa.org

American College of Obstetricians and Gynecologists (ACOG)
409 Twelfth Street SW, PO Box 96920
Washington, DC 20090-6920
www.acog.org

Kinsey Institute for Research in Sex, Gender, and Reproduction
Morrison 313, Indiana University
Bloomington, IN 47405
812-855-7686
www.kinseyinstitute.org

La Leche League International
1400 North Meacham Road
Schaumburg, IL
847-519-7730
www.lalecheleague.org

March of Dimes
1275 Mamaroneck Avenue
White Plains, NY 10605
www.marchofdimes.com

National Institute of Child Health and Human Development (NICHD)
US National Institutes of Health (NIH)
PO Box 3006
Rockville, MD 20847
800-370-2843
TTY: 888-320-6942
www.nichd.nih.gov

National Women's Health Information Center
US Department of Health and Human Services (HHS)
Office on Women's Health
800-994-9662
TTD: 888-220-5446
www.4women.gov

North American Menopause Society
5900 Landerbrook Drive, Suite 195
Mayfield Heights, OH 44124
440-442-7550
www.menopause.org

Planned Parenthood Federation of America
434 West 33rd Street
New York, NY 10001
212-541-7800
www.plannedparenthood.org

Psychiatric Disorders and Psychologic Conditions

American Academy of Child and Adolescent Psychiatry (AACAP)
3615 Wisconsin Avenue NW
Washington, DC 20016-3007
202-966-7300
www.aacap.org

American Psychiatric Association (APA)
1000 Wilson Boulevard, Suite 1825
Arlington, VA 22209
703-907-7300
www.healthyminds.org

Depression and Bipolar Support Alliance (DBSA)
730 North Franklin Street, Suite 501
Chicago, IL 60610-7224
800-826-3632
www.dbsalliance.org

National Alliance for the Mentally Ill (NAMI)
Colonial Place Three
2107 Wilson Boulevard, Suite 300
Arlington, VA 22201-3042

800-950-NAMI (6264)
www.nami.org

National Institute of Mental Health (NIMH)
US National Institutes of Health (NIH)
Public Information and Communications
6001 Executive Boulevard, Room 8184, MSC 9663
Bethesda, MD 20892-9663
301-443-4513 / 866-615-6464
TTY: 301-443-8431 / 866-415-8051
www.nimh.nih.gov

National Mental Health Association (NMHA)
2001 North Beauregard Street, 12th Floor
Alexandria, VA 22311
800-969-NMHA (6642)
www.nmha.org

VOLUME 4

Preventive Medicine

Agency for Toxic Substances and Disease Registry (ATSDR)
Division of Toxicology
US Centers for Disease Control and Prevention (CDC)
1600 Clifton Road NE, Mailstop F-32
Atlanta, GA 30333
888-42-ATSDR (888-422-8737)
www.atsdr.cdc.gov

Healthy People 2010
www.healthypeople.gov

National Center for Injury Prevention and Control
US Centers for Disease Control and Prevention (CDC)
4770 Buford Highway NE, Mailstop K65
Atlanta, GA 30341-3724
770-488-1506
www.cdc.gov/ncipc

National Institute for Occupational Safety and Health (NIOSH)
US Centers for Disease Control and Prevention (CDC)
4676 Columbia Parkway
Mail Stop C-18
Cincinnati, OH 45226
800-356-4674
www.cdc.gov/niosh

National Safety Council
1121 Spring Lake Drive
Itasca, IL 60143-3201
630-285-1121
www.nsc.org

Occupational Safety & Health Administration (OSHA)
US Department of Labor
200 Constitution Avenue
Washington DC 20210
202-693-1999 / 800-321-OSHA (6742)
www.osha.gov

US Centers for Disease Control and Prevention (CDC)
1600 Clifton Road
Atlanta, GA 30333
404-639-3534 / 800-311-3435
www.cdc.gov

US Environmental Protection Agency (EPA)
Ariel Rios Building
1200 Pennsylvania Avenue NW
Washington, DC 20460
202-272-0167
www.epa.gov

Alternative and Complementary Approaches

American Association of Naturopathic Physicians (AANP)
3201 New Mexico Avenue NW #350
Washington, DC 20016
202-895-1392 / 866-538-2267
www.naturopathic.org

National Center for Complementary and Alternative Medicine (NCCAM)
NCCAM Clearinghouse
PO Box 7923
Gaithersburg, MD 20898
888-644-6226
TTY: 866-464-3615
www.nccam.nih.gov

Genetics and Molecular Medicine

National Human Genome Research Institute (NHGRI)
US National Institutes of Health (NIH)
Building 31, Room 4B09
31 Center Drive, MSC 2152
9000 Rockville Pike
Bethesda, MD 20892-2152
301-402-0911
www.genome.gov

National Institute of General Medical Sciences (NIGMS)
US National Institutes of Health (NIH)
45 Center Drive, MSC 6200
Bethesda, MD 20892-6200
301-496-7301
www.nigms.nih.gov

United Mitochondrial Disease Foundation
8085 Saltsburg Road, Suite 201
Pittsburgh, PA 15239
412-793-8077
www.umdf.org

Drugs

National Council on Patient Information and Education (NCPIE)
4915 Saint Elmo Avenue, Suite 505
Bethesda, MD 20814-6082
301-656-8565
www.talkaboutrx.org

Nutrition and Diet

American Dietetic Association
216 West Jackson Boulevard
Chicago, IL 60606-6995
800-877-1600
www.eatright.org

US Department of Agriculture (USDA)
1400 Independence Avenue SW
Washington DC 20250
www.usda.gov

Fitness: Exercise and Health

American College of Sports Medicine (ACSM)
401 West Michigan Street
Indianapolis, IN 46202-3233
317-637-9200
www.acsm.org

President's Council on Physical Fitness and Sports
US Department of Health and Human Services (HHS)
Department W
200 Independence Avenue SW, Room 738-H
Washington, DC 20201-0004
202-690-9000
www.fitness.gov

Human Relations

APA Lesbian, Gay, and Bisexual Concerns Program
American Psychiatric Association
750 First Street NE
Washington, DC 20002
202-336-6050
www.apa.org/pi/lgbc/

National Gay and Lesbian Task Force
2320 Seventeenth Street
Washington, DC 20009
202-332-6483
www.thetaskforce.org

Parents, Families and Friends of Lesbians and Gays (PFLAG)
1726 M Street NW, Suite 400
Washington, DC 20036
202-467-8180
www.pflag.org

Sexuality Information and Education Council of the United States (SIECUS)
130 West 42nd Street, Suite 350
New York, NY 10036
212-819-9770
www.siecus.org

Surgery

American Academy of Cosmetic Surgery
737 North Michigan Avenue, Suite 2100
Chicago, IL 60611-5405
312-981-6760
www.cosmeticsurgery.org

American Academy of Facial Plastic and Reconstructive Surgery (AAFPRS)
310 South Henry Street
Alexandria, VA 22314
703-299-9291 / 800-332-FACE (800-332-3223)
www.aafprs.org

Lifestyle Variables: Smoking and Obesity

American Obesity Association
1250 Twenty-fourth Street NW, Suite 300
Washington, DC 20037
202-776-7711
www.obesity.org

SmokeFree.gov
A Web-based partnership of the American Cancer Society (ACS), CDC Office on Smoking and Health, and the National Cancer Institute (NCI).
800-QUITNOW (800-784-8669)
TTY: 800-332-8615
www.smokefree.gov

Tobacco Control Research Branch
NCI Division of Cancer Control and Population Sciences National Cancer Institute
US National Institutes of Health (NIH)
6130 Executive Boulevard, Room 6134
Executive Plaza North
Rockville, MD 20852
301-594-6776
www.tobaccocontrol.cancer.gov

Tobacco Information and Prevention Source (TIPS)
Office on Smoking and Health (OSH)
National Center for Chronic Disease Prevention and Health Promotion
US Centers for Disease Control and Prevention (CDC)
www.cdc.gov/tobacco/index.htm

Substance Abuse

National Council on Alcoholism and Drug Dependence, Inc.
22 Cortlandt Street, Suite 801
New York, NY 10007-3128
212-269-7797
www.ncadd.org

National Institute on Alcohol Abuse and Alcoholism (NIAAA)
US National Institutes of Health (NIH)
5635 Fishers Lane, MSC 9304
Bethesda, MD 20892-9304
www.niaaa.nih.gov

National Institute on Drug Abuse (NIDA)
US National Institutes of Health (NIH)
6001 Executive Boulevard, Room 5213
Bethesda, MD 20892-9561
301-443-1124
www.nida.nih.gov

Substance Abuse and Mental Health Services Administration
US Department of Health and Human Services (HHS)
1 Choke Cherry Road
Room 8-1036
Rockville, MD 20857
crisis hotline: 800-273-8255
TTY crisis hotline: 800-799-4889
www.samhsa.gov

Emergency and First Aid

American Red Cross
2025 East Street NW
Washington, DC 20006
202-303-4498
www.redcross.org

APPENDIX VII
BIOGRAPHIES OF NOTABLE PERSONALITIES

Auenbrugger, [Josef] Leopold (1722–1809) Austrian physician, also known as Leopold von Auenbrugg, who developed chest percussion as a diagnostic method. Auenbrugger recognized that fluid accumulations in the tissues changed the densities of the structures and consequently their tonal qualities. The method became a mainstay of diagnosis for cardiomyopathy (enlargement of the heart characteristic of heart failure) and lung conditions such as pulmonary edema, pneumonia, and tuberculosis.

Avicenna (980–1037) Persian physician and philosopher, also known as Ibn Sina, who earned recognition and fame before he turned 20 for his gifts as a healer. Among Avicenna's numerous writings was *The Canon of Medicine (Canticum de medicina),* 14 volumes that covered health, disease, treatment, and prevention. *The Canon of Medicine* was a primary medical text throughout Europe from the 11th to the 17th century.

Axelrod, Julius (1912–2004) American research scientist who discovered the reuptake process of the brain neurotransmitters epinephrine and norepinephrine, work for which he received a share of the Nobel Prize for Physiology or Medicine in 1970. Axelrod also conducted key research of the pineal gland, contributing to understanding of the hormone melatonin, and of analgesic medications (pain relievers), contributing to the discovery of acetaminophen.

Banting, Frederick (1891–1941) Canadian physician and researcher who, with medical student Charles Best and physician John Macleod, discovered insulin and its connection to diabetes. Banting and Macleod shared the Nobel Prize in Physiology or Medicine in 1923 for this discovery.

Barnard, Christiaan (1922–2001) South African surgeon who performed the first human heart transplant operation in 1967. Barnard transplanted the heart of a young woman who received fatal injuries in an auto accident, Denise Darvall, into the chest of Louis Washkansky, a 55-year-old dentist in the end stages of heart failure. Washkansky lived only 18 days with his new heart before dying of pneumonia; however, by the 1990s heart transplantation became the standard of care for end-stage heart failure. During his career Barnard pioneered numerous surgical techniques and devices for heart surgery.

Beaumont, William (1785–1853) US Army surgeon who studied the workings of the stomach through a healed gunshot wound that left an opening into the stomach of his patient Alexis St. Martin. Beaumont used the opening to observe the processes of the stomach's stages of digestion. Beaumont collected samples of "gastric juices" and analyzed them, discovering the chemical composition of stomach acid to be primarily hydrochloric acid. Beaumont detailed his experiments and findings in his book *Experiments and Observations on the Gastric Juice and the Physiology of Digestion* published in 1833.

Bernard, Claude (1813–1878) French physiologist who studied and documented numerous dimensions of human physiology, key among them the functions of the pancreas in digestion and the discovery of vasomotor nerves (nerves that cause blood vessels to dilate or constrict). Bernard's most significant postulation was that the interior environment of the human body remained stable relative to the external environment. This postulation became the foundation for the contemporary concept of homeostasis.

Best, Charles (1899–1978) Canadian medical student whose work with physician Frederick Banting resulted in the discovery of insulin.

Though Best did not receive a share of the Nobel Prize in Physiology or Medicine in 1923 awarded to Banting and another collaborator, John Macleod, Banting protested and shared his portion of the award money with Best. Best pursued a career in medical research that resulted in numerous other honors including induction into the Canadian Medical Hall of Fame.

Blackwell, Elizabeth (1821–1910) First woman to earn a medical degree from an American medical school. Blackwell was born in England and came with her family to the United States in 1832. She graduated with a doctor of medicine degree from Geneva Medical College in New York in 1849. Though she wanted to become a surgeon, an infection that cost her the vision in one eye forced her to change direction to specialize in obstetrics and gynecology. Blackwell founded the New York Infirmary for Women and Children in 1857 and 10 years later opened an affiliated medical school for women. During her career Blackwell wrote several influential medical texts about women's health and diseases.

Blalock, Alfred (1899–1964) American heart surgeon who pioneered numerous techniques, devices, and instruments to repair congenital heart defects. Blalock's interest in the heart came about as a result of his research to investigate and find treatments for cardiovascular shock. Blalock and his assistant, Vivien Thomas, subsequently turned their interest and methods to create surgical repairs for otherwise fatal "blue baby" heart defects, notably tetralogy of Fallot. Blalock performed the first successful such operation in 1944 on a patient of pediatrician Helen Taussig. Blalock's collaborations with other researchers resulted in operations for coarctation of the aorta and transposition of the great arteries, two other severe congenital heart defects.

Broca, Pierre Paul (1824–1880) French surgical pathologist and medical researcher best known for his study of brain anatomy and physiology. Broca identified the region of the brain's frontal lobe that controls speech, now known as Broca's area. Broca also studied correlations between brain structure and intelligence, developing numerous methods for measuring the convolutions and size of human and other primate brains, and was a prolific writer.

Chain, Ernst (1906–1979) German-born biochemist who shared the Nobel Prize in Physiology or Medicine in 1945 with Alexander Fleming and Howard Florey. The award honored the work of the three in the discovery and uses of penicillin. Chain developed methods to analyze natural antibacterial substances and discovered the process by which penicillin killed bacteria.

Charcot, Jean Martin (1825–1893) French physician who identified multiple sclerosis.

Cooley, Denton (b. 1920) American cardiovascular surgeon renowned for his skill and innovation in operations on the heart. As an intern Cooley assisted pediatric heart surgeon Alfred Blalock in the first operation to correct a congenital heart malformation ("blue baby" syndrome). Cooley spent much of his surgical career perfecting techniques that would extend the ability to surgically repair such defects. He was one of the first American cardiovascular surgeons to perform a human heart transplantation (in 1968) and to implant an artificial heart as a bridge to transplantation (in 1969). Cooley also pioneered and perfected coronary artery bypass graft (CABG).

Crick, Francis (1916–2004) British scientist who co-discovered, with American zoologist James Watson, the structure of DNA in 1953. Crick and Watson, along with biophysicist Maurice Wilkins, received the Nobel Prize in Physiology or Medicine in 1962 for the discovery. Crick devoted the remainder of his research career to studies of protein synthesis and genetic code.

de Graaf, Regnier (1641–1673) Dutch anatomist who published the first detailed studies of the male and female reproductive systems. The egg-bearing follicles on the ovaries, which de Graaf identified and described, are called Graafian follicles.

de Luzzi, Mondinus (1275–1326) Italian anatomist whose book *Anathomia*, published in 1316, was the first detailed textbook of anatomy of what medical historians consider modern Western medicine. Though heavily framed within the teachings of Galen, *Anathomia* presented de Luzzi's observations from the numerous autopsies he performed as a professor at Bologna.

DeVries, William (b. 1943) American heart surgeon best known for implanting the first artificial heart into retired dentist Barney Clark in

1982, an experimental procedure that unfolded in full public scrutiny via television. People around the world were simultaneously captivated and repulsed during the four months Clark survived with the device in his chest attached by six feet of tubing to an external and noisy pump the size of a washing machine. DeVries worked closely with Robert Jarvik, the pump's designer, and physician-inventor Willem Kolff, on the mechanical heart's design. After Clark, DeVries implanted mechanical hearts into four other people. DeVries retired from cardiovascular surgery in 1999.

Ehrlich, Paul (1854–1915) German bacteriologist and physician whose extensive research on immunity resulted in developing salvarsan, the first successful treatment for syphilis, and earned him the Nobel Prize for Physiology or Medicine in 1908. Ehrlich's studies of cell structure and function later became the foundation of chemotherapy as a treatment for cancer.

Einthoven, Willem (1860–1927) Dutch physician and scientist whose penultimate achievement was the development of the electrocardiogram (ECG) in 1903. The importance of this device for measuring and visually representing the electrical activity of the heart became apparent over the next two decades. Einthoven received the Nobel Prize in Physiology or Medicine in 1924 to honor the discovery.

Elion, Gertrude (1918–1999) American chemist who developed the first chemotherapy agents successful in treating childhood leukemia, an achievement for which she received the Nobel Prize in Physiology or Medicine in 1988 (shared with her collaborator, chemist George H. Hitchings, and chemist James W. Black who won for his work to develop beta blockers and histamine H_2 blockers). Elion developed other drugs that, although ineffective as treatments for leukemia, became therapies for immunosuppression (azathioprine) and gout (allopurinol).

Fleming, Alexander (1881–1955) Scottish bacteriologist credited with the discovery of penicillin and its actions to kill pathogenic microbes. Fleming shared, with Ernest Chain and Howard Florey, the Nobel Prize in Physiology or Medicine in 1945 for his work with penicillin. Fleming devoted his career to the study of antisepsis and wrote prodigiously of his work.

Florey, Howard Walter (1898–1968) Australian research pathologist whose work to investigate the actions of penicillin earned him a share of the Nobel Prize in Physiology or Medicine in 1945, with Alexander Fleming and Ernest Chain. Florey worked to produce large quantities of penicillin for use as an antibiotic at the end of World War II. He co-authored numerous books during his career.

Freud, Sigmund (1856–1939) Austrian psychiatrist who developed the method of psychoanalysis. As a physician Freud specialized in emotional disorders, such as neurosis, and became intrigued with the nature of the unconscious mind. He studied dreams, forgetfulness, and inadvertent comments ("Freudian slips")—all of which he perceived as insights into the workings of the mind. Freud also correlated much of the mind's functions with sexuality. Freud wrote extensively of his findings and theories, some of which remain controversial and highly debated even today. However, Freud remains the founder of psychiatry, and his work continues to provide insights for medical researchers interested in understanding the link between body and mind.

Galen, Claudius (129–199) A physician and philosopher, also called Galen of Pergamum, whose observations and study of the human body framed the practice of medicine until the Middle Ages. Galen drew much of his information from dissections of animals such as pigs and apes, however, which resulted in some fundamental errors in understanding of human anatomy and physiology. Galen also embraced the premise of the four humors (blood, phlegm, yellow bile, and black bile), in which illness and disease resulted from imbalances among these vital substances.

Gibbon, John H. Jr. (1904–1973) American physician and thoracic surgeon who developed the cardiopulmonary bypass machine, the first successful use of which took place in 1953. Gibbon continued to perfect the design and methods for using cardiopulmonary bypass, making possible the many advances in surgical operations on the heart that occurred through the latter half of the 20th century.

Gray, Henry (1825–1861) English physician, anatomist, and physiologist best known for his landmark work *Gray's Anatomy.* This extraordinary detailed description of the human body's structure

and function was first published in 1864 and remains the standard text today for medical students and other students of the medical arts. Gray taught at St. George's Hospital Medical School in London and originally produced his anatomy book to serve as a textbook for his students.

Hales, Stephen (1677–1761) English physiologist who developed a method for measuring arterial blood pressure. Hales's method required inserting a glass tube into an artery and measuring the level to which blood rose within it. Though this method was not practical from a clinical perspective, doctors soon realized the value of blood pressure as a diagnostic marker and researchers developed less intrusive methods for its measurement. Hales also conducted the first measure of a heart's capacity by filling the chambers of a freshly slaughtered sheep's heart with molten wax.

Hall, Marshall (1790–1857) English physician who discovered capillaries and their role in blood circulation. Hall also developed the first method of resuscitation for drowning victims.

Harvey, William (1578–1657) English physician who determined the flow of blood through the body's circulation to be a closed system, with the heart and lungs at its core. Harvey broke with the Galenic understanding that defined medical knowledge at the time, testing his theories extensively before releasing them in the 1628 manuscript that profoundly changed understanding of the human body: *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus (An Anatomical Exercise on the Motion of the Heart and Blood in Animals).*

Havers, Clopton (1650–1701) English physician and physiologist who was the first to document detailed microscopic descriptions of the tubular structure of compact bone, now known as the Haversian system.

Hippocrates (460–400 B.C.E.) Greek physician widely credited with establishing the tenets of modern medicine. A keen observer, Hippocrates developed numerous diagnostic and therapeutic methods and the philosophy that the physician "first and foremost, do no further harm" when treating patients. Hippocrates advanced the premise of treating the body as a whole rather than isolating and treating its symptoms.

Ibn Al-Nafis (1213–1288) Islamic physician who discovered the circulation of the blood, though his writings did not emerge into the mainstream of Western medicine for several centuries because there was little contact between East and West during his lifetime.

Ingrassias, Giovanni (1510–1580) Italian physician and anatomist who identified the smallest bone in the body, the inner ear's stapes, and a pair of small bones at the back of the eye socket that bear his name, the processes of Ingrassias.

Jarvik, Robert (b. 1946) American physician and researcher who developed a series of mechanical hearts in the 1970s and 1980s. In the first operation of its kind cardiac surgeon William DeVries implanted a Jarvik-7 mechanical heart (which Jarvik developed in collaboration with heart surgeon Willem Kolff) into retired dentist Barney Clark in 1982. Though heart surgeons eventually implanted Jarvik-7 mechanical hearts into about six dozen people, complications were extensive and quality of life was poor. In 1990 the US Food and Drug Administration (FDA) withdrew approval for human use of the mechanical heart.

Jenner, Edward (1749–1823) British physician who developed the smallpox vaccine and the process of vaccination in 1796. A country doctor in rural England, Jenner observed that dairymaids who recovered from cowpox infection did not again get the disease and furthermore did not get smallpox, a deadly or disfiguring infection that researchers later identified as being caused by a related virus. At the time the process for inducing immunity to smallpox, called variolation, was nearly as hazardous as the disease itself. Jenner instead variolated people with cowpox, a milder disease. This form of vaccination rapidly replaced variolation and became mandatory in England, significantly reducing smallpox infection and leading to improved vaccination methods that would eventually eradicate smallpox worldwide.

Jerne, Niels (1911–1994) Danish immunologist who proposed the theories that led to the development of methods to produce monoclonal antibodies (MAbs), specifically targeted immune substances now used as treatment for certain cancers and other diseases. Jerne received a share of the Nobel Prize in Physiology or Medicine in 1984 for his work.

Julian, Percy (1899–1975) African American research chemist who developed a method to syn-

thesize (create in the laboratory) cortisone, a natural hormone of the adrenal glands. Julian's methods also made possible the synthesis of other hormones for therapeutic applications, such as oral contraceptives (birth control pills) and immunosuppressive drugs.

Jung, Carl (1875–1961) Swiss psychiatrist, once a protégé of Austrian psychiatrist Sigmund Freud, who developed a theory of personality based on the premise of a collective unconscious, a pool of inborn recognitions and experiences. The collective unconscious, in Jung's view, explained commonalities across human populations in dreams, mythology, and religion. Jung identified these commonalities as archetypes, which he defined as unlearned experiences.

Koch, [Heinrich Herman] Robert (1843–1910) German bacteriologist who discovered the pathogenic nature of bacteria and the bacterium responsible for causing tuberculosis. Koch received the Nobel Prize in Physiology or Medicine in 1905 for his work in understanding the infectious mechanisms of tuberculosis. Koch made further numerous contributions to the discovery of the role of pathogenic microbes and disease.

Kolff, Willem J. (b. 1911) Physician and medical inventor who founded the first European blood bank during World War II and developed the first artificial kidney a few years later. A pioneer in devices for the heart, Kolff devised an implantable mechanical heart in 1955 and an intra-aortic balloon pump in 1957. In the 1970s and 1980s Kolff collaborated with Robert Jarvik to develop a series of mechanical hearts. Heart surgeon William DeVries implanted one model, the Jarvik-7, into the chest of retired dentist Barney Clark in 1982. Clark lived for four months on the artificial heart. Kolff also developed a portable kidney dialysis unit.

Laënnec, René (1781–1826) French physician who invented the stethoscope to listen to the heart and lungs. Laënnec's early stethoscopes were straight tubes carved of wood. Later models incorporated brass fittings to better hear certain ranges of sounds.

Landsteiner, Karl (1868–1943) Austrian scientist who discovered the antigens on the surfaces of blood cells that led to the identification of blood types. The discovery earned Landsteiner the 1930 Nobel Prize for Physiology or Medicine.

Lister, Joseph (1827–1912) British surgeon responsible for implementing methods of antisepsis to prevent infection during and after surgical operations. Lister built on the foundations that Louis Pasteur's work established, implementing a routine of cleaning surgical and traumatic wounds with carbolic acid to kill any bacteria present. He also applied antiseptic methods to cleaning surgical instruments and maintaining a clean operating field, turning surgery from an approach of last resort to a successful therapeutic method.

Macleod, John James Richard (1876–1935) Co-discoverer, with Frederick Banting and Charles Best, of insulin. Macleod and Banting won the Nobel Prize in Physiology or Medicine in 1923 for their research. While Banting shared his Nobel Prize money with Charles Best, whom he felt was slighted in being not similarly honored, Macleod shared his with the young chemist James Bertram (J.B.) Collip, who had acquired a steady supply of insulin for the team's research.

Maimonides, Moses (1135–1204) Jewish physician and rabbi, also known as Moshe ben Maimon, who was the first of four generations of his family to serve as court physician for the sultans of Egypt. Maimonides established a practice of medicine that integrated body, mind, and spirit, blending the most advanced scientific knowledge of his time with meditation and prayer.

Paré, Ambroise (1510–1590) French battlefield surgeon considered the father of trauma surgery. Paré developed numerous techniques for rapid and humane treatment with an orientation toward eventual recovery and return to productivity through the use of prosthetic limbs and other devices. Paré served as court surgeon to four French kings.

Pasteur, Louis (1822–1895) French biochemist who recognized that pathogenic microbes, notably bacteria, caused infection. Pasteur developed what became known as the germ theory of disease, establishing an understanding of the causes of infection fundamental to developing methods for treating and preventing infection. Pasteur's work became the foundation for antisepsis, vaccination, and pasteurization, all methods for preventing infection. Pasteur further discov-

ered the bacterial cause of rabies and developed the first vaccine to prevent the fatal infection in dogs, the primary source of rabies in his time, as well as in people bitten by rabid dogs.

Pavlov, Ivan (1849–1936) Russian scientist best known for his research on conditioned reflexes, in which he trained dogs to expect food when he rang a bell. Pavlov observed that after a time the dogs began to salivate when they heard the bell ring, altering the body's normal physiologic response to salivate at the sight and smell of food. Pavlov also used surgical gastric fistulas in dogs (operations to create openings into the stomach) to study the physiology of digestion, research for which he won the 1904 Nobel Prize in Physiology or Medicine.

Piaget, Jean (1896–1980) Swiss psychologist who developed numerous theories about human intelligence, the foundation of which centered around his belief of intelligence as a process of adaptation within genetically defined frameworks. Piaget defined this process through four stages beginning at birth and culminating in adolescence, with completion of one stage crucial to entering the next.

Prusiner, Stanley (b. 1942) American neurologist and biochemist who discovered prions, infectious protein fragments that cause progressive, degenerative brain diseases such as kuru disease, Creutzfeldt-Jakob disease (CJD), and variant CJD (vCJD) arising from infection with bovine spongiform encephalopathy (BSE; commonly called mad cow disease). Prusiner received the Nobel Prize in Physiology or Medicine in 1997 for his discovery and work in understanding the infectious mechanisms of prions.

Roëntgen, Wilhelm (1845–1923) German physicist who discovered X-rays and the process for using them to create images, called roentgenograms, which revealed internal structures of density such as the bones. Roëntgen received the Nobel Prize in Physiology or Medicine in 1901 for his discoveries.

Sabin, Florence (1871–1953) American physician who was the first woman to become a full professor at Johns Hopkins Medical School. Sabin conducted research that resulted in significant findings about the structure of the brain, fetal development of the lymphatic system, and tuberculosis infection. In the latter years of her medical career Sabin turned her efforts to public health in her home state of Colorado.

Salk, Jonas (1914–1995) American physician who developed the first polio vaccine, released in 1955 after eight years of research. Polio vaccination has eradicated poliomyelitis, once one of the most debilitating and often fatal infections, from much of the world.

Semmelweis, Ignaz Philipp (1818–1861) Hungarian physician who recognized the connection between puerperal fever (childbirth fever) and the then-common practice physicians followed of moving between autopsies on women who died and women who had just given birth. Semmelweis implemented stringent antisepsis procedures at the hospital where he worked, requiring physicians to wash their hands with chlorinated lime before examining patients. As a result the death rate dropped to nearly zero. Though the established medical community was slow to embrace this revolutionary change, antiseptic hand washing eventually became standard practice.

Soper, Fred (1893–1977) American epidemiologist who organized vector-eradication programs worldwide to eliminate diseases such as malaria, yellow fever, and hookworm infestation.

Taussig, Helen (1898–1986) American pediatrician and cardiologist who worked with heart surgeon Alfred Blalock and surgical researcher Vivien Thomas to develop an operation to correct severe congenital defects of the heart. The first such operation, the Blalock-Taussig procedure, was a shunt that restored the flow of blood through the lungs in defects such as tetralogy of Fallot. Taussig overcame a severe hearing loss suffered in childhood as well as bias that prevented women from obtaining medical degrees at most medical schools in the United States.

Thomas, Vivien (1910–1985) African American researcher who collaborated with heart surgeon Alfred Blalock and pediatrician Helen Taussig to develop the operative procedures and instruments to correct congenital heart defects. Intending himself to become a physician, Thomas lost his savings in the stock market crash of 1929 that ushered in the American Great Depression. By the time he recovered financially, changing educa-

tional standards and racial discrimination in combination proved too formidable for Thomas to follow his dream. Blalock nonetheless insisted that Thomas assist him in the operating room, and often Thomas guided Blalock through difficult aspects of the operations Thomas devised.

van Leeuwenhoek, Antonie (1632–1723) Dutch amateur scientist who built his own microscopes. His studies were among the earliest to detail the structures and functions of blood cells, bacteria, and sperm. The work of van Leeuwenhoek also established the role of bacteria in causing illness, providing the foundation for the research more than a century later of Robert Koch and Joseph Lister.

Vesalius, Andreas (1514–1564) Flemish anatomist whose book *De Humanis Corporis Fabrica (On the Workings of the Human Body)* was the foundation of human anatomy for centuries. Through a friendship with a judge, Vesalius gained access to the bodies of executed criminals for dissection. Many of Vesalius's discoveries contradicted the teachings of Galen, still popular at the time. Key among them were that the heart had four chambers, not two as Galen asserted, and that the major blood vessels arose from the heart, not the liver. Vesalius also provided correct and detailed drawings of the gastrointestinal structures.

von Behring, Emil Adolf (1854–1917) Prussian physician whose research on toxins and antitoxins led to the development of tetanus and diphtheria vaccines, established the foundation for serum therapy, and earned the first Nobel Prize for Physiology or Medicine awarded in 1901.

Waksman, Selman (1888–1973) Biochemist who discovered the antibiotic medications streptomycin, the first antibiotic effective for treating tuberculosis, and neomycin. Waksman received the 1952 Nobel Prize in Physiology or Medicine in recognition of his work.

Watson, James (b. 1928) American scientist who co-discovered, in collaboration with British researcher Francis Crick, the double helix structure of DNA in 1953. Watson and Crick shared the 1962 Nobel Prize in Physiology or Medicine for their work. Watson conducted much research on the role of RNA in viruses and served as director of the Human Genome Project from 1989 to 1992. He wrote several books, among them the 1968 best-seller *Double Helix,* which chronicled the discovery of DNA.

Yalow, Rosalyn (b. 1921) American physicist who developed techniques to use radioisotopes to measure the amount of peptide hormones such as insulin in the blood, which are present in very small quantities. These techniques became known as radioimmunoassays (RIAs) and are today the basis for such measurements. Yalow received a share of the Nobel Prize in Physiology or Medicine in 1977 for her work.

APPENDIX VIII
DIAGNOSTIC IMAGING PROCEDURES

Diagnostic imaging procedures offer noninvasive approaches for visualizing the structure and function of internal organs. Though each procedure has specific applications and diagnostic value, doctors often use procedures in combination with one another to give detailed information to help diagnose health conditions as well as monitor the effectiveness of treatment. Some procedures involve the injection or consumption of radioopaque contrast media (special dyes) or radioisotopes to create dimensional images.

The entries in this appendix discuss procedures that have broad application across body systems and health conditions. Entries for diagnostic imaging procedures specific to a particular body system are in the section of *The Facts On File Encyclopedia of Health and Medicine* that covers that body system. For example, MAMMOGRAM—X-RAY of the breast—appears in the section "The Reproductive System" and INTRAVENOUS PYELOGRAM (IVP)—imaging of the KIDNEYS—appears in the section "The Urinary System."

computed tomography (CT) scan A radiologic procedure that uses multiple X-RAY images to create multi-dimensional pictures of the structure of internal organs. The CT scanner takes numerous X-ray "slices" that a computer then assembles into an image of the organ or structure. The X-ray tube rotates within the scanner, moving around area of the body being scanned. A CT scan may be done with or without contrast media, depending on the reason for the procedure. CT scan of the abdomen may require a bowel prep (laxative or enema). Most other CT scans do not require any advance preparation.

The scan itself is painless, though some people may feel claustrophobic when inside the scanner. Some CT scanners are open, which reduces the sense of being closed in. Most often it is necessary to change out of regular clothing into a hospital gown for the scan, to prevent interference from objects such as zippers and buttons. A CT scan generally takes between 15 minutes and an hour, depending on the type of images the doctor desires. No recovery is necessary; when the radiologist is satisfied with the quality of images, the person may get dressed and leave.

There is a slight risk of an adverse or allergic reaction to contrast dye, which is iodine-based. CT scan does expose a person to ionizing radiation, though for most procedures the level of exposure is within the established safety boundaries. Frequent CT scans or complex CT scans, such as cardiac multislice CT (CMCT), result in significantly higher exposure, however. It is important to discuss the potential risks of such exposure before undergoing the procedure.

Doctors may order CT scans to evaluate STROKE and TRAUMATIC BRAIN INJURY (TBI), complex or questionable BONE fractures, internal masses that could be tumors, and damage to the HEART after HEART ATTACK. Certain surgeries that require extraordinary precision, such as operations on the BRAIN (for example, THALAMOTOMY and PALLIDOTOMY), may use CT scan to guide the placement of surgical instruments.

magnetic resonance imaging (MRI) An imaging procedure that uses powerful magnetic energy to visualize internal organs and structures. MRI does not involve exposure to radiation. The nuclei of hydrogen atoms (a component molecule of water) align themselves in a known pattern within the body's natural magnetic field. The MRI machine emits a strong pulse of electromagnetic energy, also called radiofrequency (RF) energy, causing the hydrogen nuclei to temporarily

realign themselves. The MRI machine then detects the rate at which the nuclei return to their natural alignment. A computer constructs multidimensional images based on this data.

MRI is particularly effective for detecting abnormal tissue within the body, such as tumors, tears to muscles, and neurologic injury or deterioration. Because of the electromagnetic disruption the MRI machine temporarily causes, people who have implanted pacemakers and other devices, metal hardware (such as to repair fractures), permanent prostheses (such as an artificial eye or COCHLEAR IMPLANT), and certain other circumstances cannot undergo MRI. It is essential to remove all clothing and items that may contain metal; the person wears a hospital gown during the procedure.

MRI is painless and takes 15 minutes to an hour depending on the area of the body being scanned. Sometimes the doctor may choose to administer an intravenous injection of a contrast medium to enhance the images the MRI produces. The MRI machine is very loud and surrounds the person during the procedure. Some people find the experience of the procedure disconcerting because of these factors. The technologist performing the MRI can provide methods to minimize this. MRI does not have any adverse side effects.

radionuclide scan A nuclear medicine procedure that measures the rate of deterioration of low-level radioactive isotopes to present images of the cellular function of organs such as the BRAIN, BONE, LIVER, THYROID GLAND, and GALLBLADDER. Radionuclide scans involve exposure to radiation. Before the scan, the person receives an intravenous injection of a small amount of fluid, typically a glucose (sugar) solution, "tagged" with the appropriate radioisotope (the radionuclide). Cells throughout the body uptake, or take in, the tagged glucose molecules. The attached radioisotope molecules deteriorate as the body uses the glucose.

Cells in various organs and structures use glucose at known rates; measuring the rate helps doctors to determine whether there is abnormal function such as tumors or healing (increased glucose use). Slowed uptake may indicate degenerative disorders or problems with healing.

During the scan the person lies on a procedure table and the gamma camera or other device passes over the area of the body being evaluated. The procedure may take 15 to 90 minutes. There is usually no need to change out of regular clothes. The risks of radionuclide scans are minimal. The radioisotopes dissipate rapidly, so the radiation does not remain in the body very long. Specialized types of radionuclide scans include positron emission tomography (PET) scan and single photon emission computed tomography (SPECT).

ultrasound Also called ultrasonography, a diagnostic procedure that uses high-frequency sound waves (beyond the frequency human hearing can detect) to create images of internal organs and structures. Ultrasound does not involve exposure to radiation. Ultrasound is painless and is especially effective for evaluating hollow structures within the body such as the GALLBLADDER, urinary BLADDER, and arteries and veins. Doppler ultrasound is a technique that presents moving images, such as the flow of BLOOD or the movement of a FETUS within a pregnant woman's uterus. Ultrasound is also useful for detecting cysts and tumors in structures such as the OVARIES, TESTICLES, BREASTS, and PROSTATE GLAND. Doctors sometimes use ultrasound to guide the placement of biopsy instruments.

Ultrasound typically requires no advance preparation, though pelvic ultrasound may require a full urinary bladder. The procedure is painless. During the procedure, the sonographer applies a warm gel to the surface of the skin over the area being scanned. The gel improves the conductivity of sound signals. The sonographer gently presses a transducer against the skin and moves it in a particular pattern. The transducer emits ultrasound waves, which "echo" from the structures within the body. The transducer then picks up the echoes and transmits them back to the ultrasound machine, which creates representational images from them.

Some ultrasound procedures involve placing the transducer within a natural body opening such as the VAGINA, RECTUM, or ESOPHAGUS to provide focused examination of key structures that are deeper within the body. Transesophageal ultrasound, for example, can provide close examination of the heart. ECHOCARDIOGRAM is another type of ultrasound that specifically examines the HEART.

X-ray A radiologic procedure to evaluate the structure of dense organs within the body such as bone. X-ray involves exposure to ionizing radiation. An X-ray machine emits a beam of ionizing radiation that tissues within the body absorb. The more dense the tissue, the more radiation it absorbs. Solid structures such as bone absorb high amounts of radiation; thus X-ray is particularly effective for detecting injuries and other abnormalities of the bones. X-ray can also detect the presence of many types of tumors because their tissues have different density than normal structures, as well as the presence of abnormal air or fluid (such as in the lungs or abdomen).

Most X-ray procedures require removing clothing that could interfere with the X-ray image, such as items that have buttons and zippers. Some X-ray procedures, such as BARIUM ENEMA, require advance preparation and the use of contrast media. Some X-ray procedures require awkward positions or holding the breath, which may be temporarily uncomfortable. Most X-ray procedures are painless, though people may feel pain from the injuries being evaluated during the procedure. Infrequent X-rays pose very little risk to health. People who need frequent X-rays should discuss the risk of radiation exposure with their doctors.

APPENDIX IX
FAMILY MEDICAL TREE

A family medical tree can help your doctor determine inherited and genetic health risks. Optimally a family medical tree includes information about the causes of death and significant medical conditions for as many family generations as possible. The most significant health information is that for first-degree relatives (siblings, parents, and children) and second-degree relatives (nephews, nieces, cousins, aunts, uncles, and grandparents). Some health information may be vague or use antiquated terminology (for example, consumption to identify tuberculosis or dropsy to identify congestive heart failure).

It is especially important to know the cause of death whenever possible, as this provides clues to underlying health conditions. For deaths occurring within the past few decades, this information appears on the death certificate. Other useful information includes any history of

- HEART disease, such as STROKE, HEART ATTACK (MYOCARDIAL INFARCTION), sudden (or unexplained) cardiac death, ATHEROSCLEROSIS, ARTERIOSCLEROSIS, CARDIOMYOPATHY (enlarged heart), congestive HEART FAILURE, PERIPHERAL VASCULAR DISEASE (PVD), DEEP VEIN THROMBOSIS (DVT), INTERMITTENT CLAUDICATION, LONG QT SYNDROME (LQTS), and ARRHYTHMIA
- congenital heart defects or disorders, including treatments (such as surgery) to repair or treat them
- CANCER, especially BREAST CANCER, COLORECTAL CANCER, OVARIAN CANCER, PROSTATE CANCER, and childhood cancers such as LEUKEMIA or WILMS'S TUMOR
- neurologic disorders such as ALZHEIMER'S DISEASE, HUNTINGTON'S DISEASE, and PARKINSON'S DISEASE
- known GENETIC DISORDERS or CHROMOSOMAL DISORDERS such as HEMOPHILIA, DOWN SYNDROME, TURNER'S SYNDROME, KLINEFELTER'S SYNDROME, or generalized BIRTH DEFECTS
- SEASONAL ALLERGIES, allergies to medications or foods, ASTHMA, or MIGRAINE HEADACHE
- INFLAMMATORY BOWEL DISEASE (IBD), SYTEMIC LUPUS ERYTHEMATOSUS (SLE), HYPOTHYROIDISM, type 1 DIABETES, RHEUMATOID ARTHRITIS, or other AUTOIMMUNE DISORDERS
- INFERTILITY, PREMATURE OVARIAN FAILURE (POF), MISCARRIAGE (spontaneous ABORTION), STILLBIRTH, breech presentation, or other difficulties with PREGNANCY and CHILDBIRTH
- type 2 DIABETES, OBESITY, or INSULIN RESISTANCE
- DEPRESSION, GENERALIZED ANXIETY DISORDER (GAD), BIPOLAR DISORDER, SCHIZOPHRENIA, SEASONAL AFFECTIVE DISORDER (SAD), LEARNING DISORDERS, or intellectual deficiency (mental retardation)
- ALCOHOLISM, SUBSTANCE ABUSE, or CIGARETTE SMOKING
- HEMOCHROMATOSIS, WILSON'S DISEASE, PHENYLKETONURIA (PKU), and other disorders of METABOLISM
- MUSCULAR DYSTROPHY or CYSTIC FIBROSIS

A family history of health conditions does not necessarily point to a personal history with the same conditions. However, it provides important clues about a person's possible predilection for such conditions. The most accurate method to

compile a family medical tree is to ask key family members, such as parents and grandparents, about health conditions. However, some people are reluctant to discuss health problems. Sometimes it is helpful to mention to the doctor that a particular health condition affects more than one first degree relative or multiple second degree relatives.

Record family health information, and give a copy of the document to the family or regular physician as well as other family members.

APPENDIX X
IMMUNIZATION AND ROUTINE EXAMINATION SCHEDULES

Preventive health examinations and immunizations are crucial for optimal health and disease resistance across the spectrum of life. Recommended schedules, examination procedures, and immunizations change as knowledge grows and new developments become available. The information in this appendix represents a composite of common recommendations current at the time of publication. Recommendations may differ according to age and between men and women.

Preventive Health Care for Infants and Children

Most health experts recommend well child examinations for basic preventive health care on a schedule frequent enough for early detection of physical or mental developmental delays and concerns. Well child exams should include age-appropriate general health measures such as

- length/height
- weight
- head circumference (infants)
- reflexes
- vital signs (heart rate, breathing rate, blood pressure, body temperature)
- basic vision and hearing screening
- scoliosis detection
- coordination, balance, and gait
- nutritional status
- appropriate immunizations

WELL CHILD EXAMINATION SCHEDULE RECOMMENDATIONS BY AGE

Infancy	
2 to 4 days after birth	10 days after birth
Early Childhood	
2 months	4 months
6 months	9 months
12 months	15 months
18 months	24 months
Middle Childhood	
3 years	4 years
5 years	6 years
8 years	10 years
Adolescence	
12 years	14 years
16 years	18 years

Immunizations and immunization schedules change as new vaccines become available. The American Academy of Pediatrics (AAP) establishes and updates recommendations. The most current immunizations and their schedules are available on the AAP's Web site (www.aap.org) as well as through public health departments and public and private health organizations.

Immunization schedules for children vary according to the age at which the child receives the first dose of a multidose vaccination series. For some immunizations there is a window of opportune timing. The pediatrician adjusts each child's schedule for appropriate timing of doses, including "catch-up" scheduling for children who begin

immunizations later than recommended. Timing and doses for each vaccine are crucial for the body's process of developing immunity. Nearly all children should receive all recommended immunizations; public schools throughout the United States require certain immunizations for school registration unless there are extenuating circumstances. Such factors vary among states.

Preventive Health Care for Adults

Preventive health-care examinations for adults vary according to gender and age. Adults also require certain immunizations. Most adults should receive a tetanus-diphtheria booster every 10 years, hepatitis B vaccine if not immunized in childhood, and influenza vaccination (flu shot) and every year.

PREVENTIVE HEALTH EXAMINATION RECOMMENDATIONS: ADULTS

Age	Well Exam Frequency	Exam Includes
19 to 39	men: every 5 years women: every 3 years	health risk screening: cholesterol, blood pressure, diabetes, sexually transmitted diseases (STDs) height/weight vital signs men: testicular exam women: breast exam, pelvic exam, Pap test
40 to 49	men: every 5 years women: every 3 years	health risk screening: cholesterol, blood pressure, diabetes, STDs, heart disease, cancer height/weight vital signs fecal occult blood test (FOBT) men: testicular exam, baseline prostate exam women: breast exam, pelvic exam, Pap test, baseline mammogram
50 to 64	men: every 3 to 5 years women: every 2 to 3 years	health risk screening: cholesterol, blood pressure, diabetes, STDs, heart disease, cancer, thyroid height/weight vital signs FOBT baseline colonoscopy, repeat every 10 years men: testicular exam, prostate exam women: breast exam, pelvic exam, Pap test annual mammogram
65 and older	men and women: every year	health risk screening: cholesterol, blood pressure, diabetes, STDs, heart disease, cancer, thyroid height/weight vital signs FOBT colonoscopy every 10 years men: prostate exam women: breast exam, pelvic exam, mammogram

APPENDIX XI
MODERN MEDICINE TIMELINE

TIMELINE OF MODERN MEDICINE

Date	Discovery	Date	Discovery
1950	penicillin, the first broad-spectrum antibiotic, became available	1976	single photon emission computed tomography (SPECT) scan; coronary artery bypass graft (CABG)
1952	polio vaccine; isoniazid developed to treat tuberculosis; first published link between cigarette smoking and lung cancer	1978	first in vitro fertilization infant born; radionuclides for diagnostic imaging
1953	first open heart surgery using a heart–lung bypass machine; DNA decoded; medical ultrasound	1980	magnetic resonance imaging (MRI); smallpox declared eradicated worldwide; first laparoscopic appendectomy
1954	first living donor kidney transplantation	1981	first heart–lung combined transplantation; hepatitis B vaccine
1959	first drug to treat leukemia	1982	acquired immunodeficiency syndrome (AIDS) identified; first permanent artificial heart implanted; first use of monoclonal antibodies (MAbs) to treat cancer
1960	first oral contraceptive (birth control pill) becomes available in the United States	1983	human immunodeficiency virus (HIV) identified as cause of AIDS
1962	oral polio vaccine	1984	first cochlear implant
1963	first cadaveric donor kidney transplantation	1985	positron emission tomography (PET) scan
1964	measles vaccine; first US Surgeon General's report on smoking and health	1986	first double-lung transplantation
1965	US Congress passes laws to establish Medicare and Medicaid programs, require warning labels on cigarette packages	1987	first small bowel transplantation
1966	first pancreas–kidney combined transplantation; first mammography machine	1988	first split-liver transplantation
1967	first human heart transplantation; first liver transplantation; mumps vaccine; kidney dialysis machine	1989	first living donor liver transplantation
1970	rubella vaccine	1990	first living donor lung transplantation
1973	DNA cloning	1994	robotic laparoscopy
1974	first disposable syringe	1995	blood substitute
1975	chorionic villi sampling (CVS)	1999	first human chromosome sequenced
		2003	human genome mapping completed

APPENDIX XII
NOBEL LAUREATES IN PHYSIOLOGY OR MEDICINE

Alfred Nobel (1833–1896), a successful Swedish businessman who invented dynamite, established the Nobel Prize in his will. Nobel intended for the prize to honor "those who, during the preceding year, shall have conferred the greatest benefit on mankind." Nobel stipulated five areas of award: physics, chemistry, physiology or medicine, literature, and peace.

The Nobel Assembly at Karolinska Institutet in Stockholm, Sweden accepts nominations—up to several hundred each year—and selects the laureates. Up to three people, working independently or in collaboration, may share the Nobel Prize in Physiology or Medicine each year. No Nobel Prize in Physiology or Medicine was awarded in 1915, 1916, 1917, 1918, 1921, 1925, 1940, 1941, and 1942.

Complete information about Nobel laureates in all categories appears on the Nobel Prize Web site (nobelprize.org).

LAUREATES, NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE

Year	Laureate(s)	Discovery
2005	Barry J. Marshall (b. 1951; Australia) J. Robin Warren (b. 1937; Australia)	*Helicobacter pylori* as the cause of peptic ulcer disease
2004	Richard Axel (b. 1946; USA) Linda B. Buck (b. 1947; USA)	mechanisms through which the sense of smell (olfactory system) recognizes and organizes odors
2003	Paul C. Lauterbur (b. 1929; USA) Sir Peter Mansfield (b. 1933; UK)	magnetic resonance imaging (MRI)
2002	Sydney Brenner (b. 1927; UK) H. Robert Horvitz (b. 1947; USA) John E. Sulston (b. 1942; UK)	how genes regulate organ development and cell apoptosis (natural cell death)
2001	Leland H. Hartwell (b. 1939; USA) Tim Hunt (b. 1943; UK) Sir Paul Nurse (b. 1949; UK)	mechanisms that control the life cycle of cells and cell division
2000	Arvid Carlsson (b. 1923; Sweden) Paul Greengard (b. 1925; USA) Eric R. Kandel (b. 1929; USA)	mechanisms by which neurotransmitters carry nerve impulses among brain neurons
1999	Günter Blobel (b. 1999; Germany)	intrinsic signals that direct proteins to their target locations within cells

Year	Laureate(s)	Discovery
1998	Robert F. Furchgott (b. 1916; USA) Louis J. Ignarro (b. 1941; USA) Ferid Murad (b. 1936; USA)	role of nitric oxide in the functions of the heart and blood vessels
1997	Stanley B. Prusiner (b. 1942; USA)	infectious prions
1996	Peter C. Doherty (b. 1940; Australia) Rolf M. Zinkernagel (b. 1944; Switzerland)	mechanisms through which the immune system recognizes and attempts to contain cells infected with viruses
1995	Edward B. Lewis (1918–2004; USA) Christiane Nüsslein-Volhard (b. 1942; Germany) Eric F. Wieschaus (b. 1947; USA)	mechanisms through which genes control the development of cells and tissues into specialized structures and organs in the embryo
1994	Alfred G. Gilman (b. 1941; USA) Martin Rodbell (1925–1998; USA)	G-proteins, which regulate how cells receive and use other protein signals
1993	Richard J. Roberts (b. 1943; UK) Phillip A. Sharp (b. 1944; USA)	split, or segmented, genes
1992	Edmond H. Fischer (b. 1920; USA) Edwin G. Krebs (b. 1918; USA)	roles of the enzymes kinase and phosphatase to attach and remove molecules for energy (glucose) release and storage
1991	Erwin Neher (b. 1944; Germany) Bert Sakmann (b. 1942; Germany)	single ion channels and their functions in cell electrical activity
1990	Joseph E. Murray (b. 1919; USA) E. Donnall Thomas (b. 1920; USA)	organ transplantation to treat diseases such as kidney failure and heart failure, including management of the immune response to prevent organ rejection and host vs. graft disease
1989	J. Michael Bishop (b. 1936; USA) Harold E. Varmus (b. 1939; USA)	origin of oncogenes is within cells that become cancerous
1988	Sir James W. Black (b. 1924; UK) Gertrude B. Elion (1918–1999; USA) George H. Hitchings (1905–1998; USA)	Black: mechanisms by which drugs are effective in treating diseases such as heart disease and cancer Elion and Hitchings: mechanisms of RNA function resulting in new drugs to treat various diseases such as leukemia, malaria, and organ rejection after transplantation
1987	Susumu Tonegawa (b. 1939; Japan)	role of genes in the production and function of antibodies
1986	Stanley Cohen (b. 1922; USA) Rita Levi-Montalcini (b. 1909; Italy)	nerve growth factor (NGF) and epidermal growth factor (EGF), substances that regulate cell growth and differentiation
1985	Michael S. Brown (b. 1941; USA) Joseph L. Goldstein (b. 1940; USA)	mechanisms that regulate cholesterol metabolism

Year	Laureate(s)	Discovery
1984	Niels K. Jerne (1911–1994; Denmark) Georges J. F. Köhler (1946–1995; Germany) César Milstein (1927–2002; Argentina)	Jerne: regulatory mechanisms of antibody production and function Köhler and Milstein: monoclonal antibodies (MAbs)
1983	Barbara McClintock (1902–1992; USA)	mobile genetic elements and genetic instability
1982	Sune K. Bergström (1916–2004; Sweden) Bengt I. Samuelsson (b. 1934; Sweden) John R. Vane (1927–2004; UK)	prostaglandins
1981	Roger W. Sperry (1913–1994; USA) David H. Hubel (b. 1926; USA) Torsten N. Wiesel (b. 1924; Sweden)	Sperry: specialized differences in the functions of the brain's hemispheres Hubel and Weisel: mechanisms through which the brain's visual cortex receives and interprets visual signals
1980	Baruj Benacerraf (b. 1920; USA) Jean Dausset (b. 1916; France) George D. Snell (1903–1996; USA)	genetic regulation of major histocompatibility complex (MHC) antigens
1979	Allan M. Cormack (1924–1998; USA) Godfrey N. Hounsfield (1919–2004; UK)	computed tomography (CT) scanning
1978	Werner Arber (b. 1929; Switzerland) Daniel Nathans (1928–1999; USA) Hamilton O. Smith (b. 1931; USA)	restrictive enzymes and their roles in genetic functions
1977	Roger Guillemin (b. 1924; USA) Andrew V. Schally (b. 1926; USA) Rosalyn Yalow (b. 1921; USA)	Guillemin and Schally: hypothalamus production of "releasing hormones" that direct the functions of other endocrine glands Yalow: radioimmunoassays to detect levels of peptide hormones in the blood circulation
1976	Baruch S. Blumberg (b. 1925; USA) D. Carleton Gajdusek (b. 1923; USA)	mechanisms through which infectious diseases originate and perpetuate
1975	David Baltimore (b. 1938; USA) Renato Dulbecco (b. 1914; USA) Howard M. Temin (1934–1994; USA)	mechanisms by which viruses interact with cell DNA and RNA to cause transformations that result in tumor development and growth
1974	Albert Claude (1899–1983; Belgium) Christian de Duve (b. 1917; Belgium) George E. Palade (b. 1912; USA)	cell components and composition and their effects on cell structure and function
1973	Karl von Frisch (1886–1982; Germany) Konrad Lorenz (1903–1989; Austria) Nikolaas Tinbergen (1907–1988; UK)	patterns of personal behaviors and social interactions as they relate to healthy and unhealthy psychosocial states
1972	Gerald M. Edelman (b. 1929; USA) Rodney R. Porter (1917–1985; UK)	chemical structures of antibody molecules

Year	Laureate(s)	Discovery
1971	Earl W. Sutherland Jr. (1915–1974; USA)	mechanisms through which hormones function in the body
1970	Sir Bernard Katz (1911–2003; UK) Ulf von Euler (1905–1983; Sweden) Julius Axelrod (1912–2004; USA)	neurotransmitters and their roles in the mechanisms through which nerve cells communicate with other cells in the body
1969	Max Delbrück (1906–1981; USA) Alfred D. Hershey (1908–1997; USA) Salvador E. Luria (1912–1991; USA)	genetic structure and replication mechanisms of viruses
1968	Robert W. Holley (1922–1993; USA) H. Gobind Khorana (b. 1922; USA) Marshall W. Nirenberg (b. 1927; USA)	role of genes in protein synthesis
1967	Ragnar Granit (1900–1991; Sweden) Haldan K. Hartline (1903–1983; USA) George Wald (1906–1997; USA)	biochemical and physiologic mechanisms involved in the eye's processing of visual input and information
1966	Peyton Rous (1897–1970; USA) Charles B. Huggins (1901–1997; USA)	Rous: viruses that cause tumors to develop Huggins: effect of therapeutic hormones on prostate cancer
1965	François Jacob (b. 1920; France) André Lwoff (1902–1994; France) Jacques Monod (1910–1976; France)	role of genes in regulating enzyme synthesis and virus replication
1964	Konrad Bloch (1912–2000; USA) Feodor Lynen (1911–1979; Germany)	relationship between metabolism of fatty acids and formation of cholesterol in the body
1963	Sir John Eccles (1903–1997; Australia) Alan L. Hodgkin (1914–1998; UK) Andrew F. Huxley (b. 1917; UK)	role of ions and ion channels in the conduction of electrical impulses through nerve cells
1962	Francis Crick (1916–2004; UK) James Watson (b. 1928; USA) Maurice Wilkins (1916–2004; UK)	double helix structure of DNA and its role in transmitting genetic and molecular information
1961	Georg von Békésy (1899–1972; USA)	mechanisms of function of the cochlea
1960	Sir Frank Macfarlane Burnet (1899–1985; Australia) Peter Medawar (1915–1987; UK)	characteristics and development of acquired immunity
1959	Severo Ochoa (1905–1993; USA) Arthur Kornberg (b. 1918; USA)	synthesis of RNA and DNA
1958	George Beadle (1903–1989; USA) Edward Tatum (1909–1975; USA) Joshua Lederberg (b. 1925; USA)	Beadle and Tatum: biochemical mechanisms of gene activity Lederberg: genetic recombination

Year	Laureate(s)	Discovery
1957	Daniel Bovet (1907–1992; Italy)	mechanisms through which certain drugs can block the actions and effects of endogenous substances
1956	André F. Cournand (1895–1988; USA) Werner Forssmann (1904–1979; Germany) Dickinson W. Richards (1895–1973; USA)	use of cardiac catheterization to diagnosis diseases of the heart and blood vessels
1955	(Axel) Hugo (Theodor) Theorell (1903–1982; Sweden)	mechanisms through which enzymes that cause oxidation function
1954	John F. Enders (1897–1985; USA) Thomas H. Weller (b. 1915; USA) Frederick C. Robbins (1916–2003; USA)	laboratory culture of the poliomyelitis virus in different kinds of tissues
1953	Hans Krebs (1900–1981; UK) Fritz Lipmann (1899–1986; USA)	Krebs: metabolic process within the cell that converts nutrients to energy (now called the Krebs cycle) Lipmann: coenzyme A and its role in cellular metabolism
1952	Selman A. Waksman (1888–1973; USA)	streptomycin, first antibiotic to treat tuberculosis
1951	Max Theiler (1899–1972; South Africa)	mechanisms of and treatment for yellow fever
1950	Edward C. Kendall (1886–1972; USA) Tadeus Reichstein (1897–1996; Switzerland) Philip S. Hench (1896–1965; USA)	isolation and functions within the body of cortisone and other hormones of the adrenal cortex
1949	Walter Hess (1881–1973; Switzerland) Egas Moniz (1874–1955; Portugal)	Hess: activities of the midbrain as they regulate the body's autonomic vital functions Moniz: prefrontal leucotomy (surgery to sever connections between regions of the brain responsible for intense emotional responses, notably anger) to treat schizophrenia
1948	Paul Müller (1899–1965; Switzerland)	use of the organic pesticide DDT to eradicate insects responsible for transmitting disease
1947	Carl Cori (1897–1984; USA) Gerty Cori (1897–1957; USA) Bernardo Houssay (1887–1971; Argentina)	Cori and Cori: conversion of glycogen to glucose Houssay: role of the hypophysis in carbohydrate metabolism and diabetes
1946	Hermann J. Muller (1890–1967; USA)	capability of X-rays to cause gene mutations
1945	Sir Alexander Fleming (1881–1955; UK) Ernst B. Chain (1906–1979; UK) Sir Howard Florey (1898–1968; Australia)	penicillin and its ability to cure infectious diseases
1944	Joseph Erlanger (1874–1965; USA) Herbert S. Gasser (1888–1963; USA)	varying conductivity and function of single fibers within nerves

Year	Laureate(s)	Discovery
1943	Henrik Dam (1895–1976; Denmark) Edward A. Doisy (1893–1986; USA)	isolation and biochemical actions of vitamin K
1939	Gerhard Domagk (1895–1964; Germany)	antibacterial actions of prontosil, particularly against streptococcal bacteria
1938	Corneille Heymans (1892–1968; Belgium)	functions of the cardio-aortic and carotid sinus areas in regulating the rate of respiration (breathing)
1937	Albert von Szent-Györgyi Nagyrapolt (1893–1986; Hungary)	metabolic functions of vitamin C
1936	Sir Henry Dale (1875–1968; UK) Otto Loewi (1873–1961; Austria)	role of neurotransmitters and other biochemicals in conducting nerve impulses
1935	Hans Spemann (1869–1941; Germany)	embryonic organizer areas that regulate how cells form tissues, organs, and structures within the developing embryo
1934	George H. Whipple (1878–1976; USA) George R. Minot (1885–1950; USA) William P. Murphy (1892–1987; USA)	consumption of animal liver as treatment for anemia
1933	Thomas H. Morgan 1866–1945; USA)	chromosomes as primary units of heredity
1932	Sir Charles Sherrington (1857–1952; UK) Edgar Adrian (1889–1977; UK)	structures and functions of neurons and nerves (afferent and efferent conductivity)
1931	Otto Warburg (1883–1970; Germany)	identification and function of hydrogen-transferring enzymes in respiration
1930	Karl Landsteiner (1868–1943; Austria)	human blood groups
1929	Christiaan Eijkman (1858–1930; Netherlands) Sir Frederick Hopkins (1861–1947; UK)	Eijkman: role of vitamins in diseases such as beriberi Hopkins: role of vitamins in growth
1928	Charles Nicolle (1866–1936; France)	transmission of typhus by the body louse
1927	Julius Wagner-Jauregg (1857–1940; Austria)	inoculation with malaria as a treatment, by inducing fever high enough to alter brain function, for psychoses
1926	Johannes Fibiger (1867–1828; Denmark)	*Spiroptera carcinoma*, a burrowing worm capable of causing cancerous tumors
1924	Willem Einthoven (1860–1927; Netherlands)	electrocardiogram (ECG)
1923	Frederick G. Banting (1891–1941; Canada) John Macleod (1876–1935; Canada)	insulin

Year	Laureate(s)	Discovery
1922	Archibald V. Hill (1886–1977; UK) Otto Meyerhof (1884–1951; Germany)	muscle metabolism and the ability of muscle activity to generate heat
1920	August Krogh (1874–1949; Denmark)	neuromuscular mechanisms that regulate capillary constriction and dilation
1919	Jules Bordet (1870–1961; Belgium)	immunity and infectious diseases
1914	Robert Bárány (1876–1936; Austria)	vestibular apparatus (receptors located within the inner ear that detect the body's position relative to the external environment)
1913	Charles Richet (1850–1935; France)	mechanisms of anaphylaxis (severe hypersensitivity reaction)
1912	Alexis Carrel (1873–1944; France)	transplantation of blood vessels and organs
1911	Allvar Gullstrand (1862–1930; Sweden)	refractive functions and errors of the eye (physiologic dioptrics)
1910	Albrecht Kossel (1853–1927; Germany)	role of proteins and nucleic acids in cellular function
1909	Theodor Kocher (1841–1917; Switzerland)	function and dysfunction of the thyroid gland
1908	Ilya Mechnikov (1845–1916; Russia) Paul Ehrlich (1854–1915; Germany)	Mechnikov: function of phagocytosis in the immune response Ehrlich: salvarsan as the first effective treatment for syphilis
1907	Alphonse Laveran (1845–1922; France)	role of protozoa in causing diseases such as malaria
1906	Camillo Golgi (1843–1926; Italy) Santiago Ramón y Cajal (1852–1934; Spain)	structure of the nervous system, notably the spinal cord and spinal nerves
1905	Robert Koch (1843–1910; Germany)	isolation and cultivation of the tubercle bacillus responsible for causing tuberculosis and the mechanisms of tuberculosis infection
1904	Ivan Pavlov (1849–1936; Russia)	physiology of digestion
1903	Niels Ryberg Finsen (1860–1904; Denmark)	therapeutic use of sunlight to treat conditions of the skin such as lupus vulgaris
1902	Ronald Ross (1857–1932; UK)	transmission of malaria by mosquito bites
1901	Emil von Behring (1854–1917; Germany)	serum antitoxin to treat diphtheria

SELECTED BIBLIOGRAPHY AND FURTHER READING

The books listed in this section can provide comprehensive information about health and medical subjects. Many are reference books that publishers periodically update and may be available in newer editions than those listed here. "Appendix VI: Resources" contains Web sites and other sources that provide the most current information about health topics, including research.

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MEDICAL ADVISORY REVIEW PANEL

Kyra J. Becker, M.D., is codirector of the University of Washington Stroke Center in Seattle, Washington. She is also an associate professor of neurology and neurological surgery at the University of Washington School of Medicine. Dr. Becker provides patient care through her practice at Harborview Medical Center and is a primary investigator on several stroke-related research studies.

Dr. Becker received her bachelor of science (B.S.) degree in biology *summa cum laude* from Virginia Tech in Blacksburg, Virginia, and her doctor of medicine (M.D.) degree from Duke University School of Medicine in Durham, North Carolina. She completed her internship in internal medicine, residency in neurology, and clinical fellowship in critical care neurology all at Johns Hopkins Hospital in Baltimore, Maryland. Dr. Becker is board-certified in neurology and psychiatry with a special certification in vascular neurology.

James C. Blair, III, PA-C, is director of Madrona Hill Urgent Care Center in Port Townsend, Washington. Mr. Blair is a physician assistant certified with special recognition in primary care and surgery. He is an advanced cardiac life support (ACLS) instructor and has worked much of his career to provide emergency services in small hospitals and clinical care settings in rural communities.

Mr. Blair received his associate of science degree in nursing from Wenatchee Valley College in Wenatchee, Washington, and completed the MEDEX Northwest Physician Assistant Program at the University of Washington School of Medicine in Seattle, Washington.

Alexa Fleckenstein, M.D., writes books and conducts lectures and workshops about natural health topics. Educated in Germany and the United States, she has extensive experience in natural therapies and integrative medicine. Dr. Fleckenstein is board-certified in internal medicine.

Dr. Fleckenstein received her medical degree from Universität Hamburg, Germany. She completed her internship and residency in primary care medicine at Carney Hospital in Boston, Massachusetts, and a fellowship in ambulatory medicine at VA Brockton, Massachusetts. Her subspecialty certification in natural medicine is from Ärztekammer Hamburg (German Board).

Nancy A. Lewis, Pharm.D., is a clinical pharmacist and medical science liaison for MGI Pharma, Inc., a biopharmaceutical company specializing in oncology and acute care products. Dr. Lewis frequently conducts workshops and focused training presentations. She is an active member of the Washington-Alaska Cancer Pain Initiative.

Dr. Lewis received her bachelor of science (B.S.) in pharmacy and her doctor of pharmacy (Pharm.D.) degrees from the University of Washington in Seattle, Washington. She serves on the clinical faculty at the University of Washington in Seattle, Washington and on the adjunct faculty at Washington State University in Pullman, Washington.

Gary R. McClain, Ph.D., is a psychologist, counselor, and consultant in New York City. Dr. McClain has more than 25 years of experience as a mental health professional and in the business world. The focus of his practice is healthcare and wellness.

Dr. McClain's graduate studies were in clinical psychology and education, with a focus on adult personality development and learning. He received his doctor of philosophy (Ph.D.) from the

University of Michigan. Dr. McClain has coauthored or edited 14 books and frequently conducts workshops.

Maureen Ann Mooney, M.D., is a clinical, surgical, and cosmetic dermatologist in private practice in Puyallup, Washington, where she specializes in treating skin cancer. Dr. Mooney is trained to perform Mohs' Micrographic Surgery. Dr. Mooney is board-certified in dermatology and dermatopathology.

Dr. Mooney received her bachelor of science (B.S.) degree in biology *summa cum laude* from the University of Minnesota College of Biological Sciences in St. Paul, Minnesota, and her doctor of medicine (M.D.) degree from the University of Minnesota School of Medicine in Minneapolis, Minnesota. She completed her internship at Hennepin County Medical Center in Minneapolis, Minnesota, and her residency in dermatology at New Jersey Medical School in Newark, New Jersey. Dr. Mooney also completed fellowships in Dermatopathology at New Jersey Medical School and Mohs' Micrographic Surgery at Louisiana State University Healthcare network in New Orleans, Louisiana.

Margaret J. Neff, M.D., M.Sc., is attending physician, pulmonary and critical care medicine, at Harborview Medical Center in Seattle, Washington. Dr. Neff is a medical monitor for the Cystic Fibrosis Therapeutic Diagnostics Network, co-chair of one of the biomedical committees of the University of Washington Institutional Review Board, and a clinical investigator on several research studies. She is board-certified in internal medicine, pulmonary disease, and critical care medicine.

Dr. Neff earned her bachelor's degree in biological sciences (B.S.) and medical degree (M.D.) from Stanford University in Stanford, California, and her master of science (M.S.) degree in epidemiology from the University of Washington in Seattle, Washington. She completed her internship and residency in internal medicine and a fellowship in intensive care at Stanford University and a fellowship in pulmonary/critical care at the University of Washington. Dr. Neff is an assistant professor of medicine in the division of pulmonary and critical care medicine at the University of Washington School of Medicine, Seattle, Washington.

Maureen Pelletier, M.D., C.C.N., F.A.C.O.G., is board-certified in obstetrics and gynecology as well as in clinical nutrition. A former aviation medical examiner, Dr. Pelletier is also licensed as a medical acupuncturist and is a DAN! (Defeat Autism Now!) physician. She is in private practice in Cincinnati, Ohio, with an emphasis on integrative medicine.

Dr. Pelletier received her medical degree (M.D.) from Tufts University School of Medicine in Boston, Massachusetts, and completed her residency in obstetrics and gynecology at the University of Cincinnati. She received clinical training in mind-body medicine at the Mind-Body Institute at Harvard University and completed the integrative medicine program at the University of Arizona School of Medicine. Dr. Pelletier is a national and international lecturer.

Otelio S. Randall, M.D., F.A.C.C., is director of the preventive cardiology program, hypertension and clinical trials, and the Cardiovascular Disease Prevention and Rehabilitation Center at Howard University Hospital in Washington, D.C. Dr. Randall is widely published in peer-reviewed journals and has authored two books. He has received numerous awards during his career, including the 2004 Outstanding Faculty Research Award from Howard University School of Medicine.

Dr. Randall received his bachelor's degree (B.S.) in chemistry from Howard University and his medical degree (M.D.) from the University of Michigan Medical School in Ann Arbor, Michigan. He completed his internship at the State University of New York at Brooklyn, residencies in internal medicine at Baylor College of Medicine in Houston, Texas, and University of Michigan Hospital, and a fellowship in cardiology at the University of Michigan Hospital. Dr. Randall is designated a specialist in hypertension by the ASH specialists program in affiliation with the American Society of Hypertension (ASH).

Susan D. Reed, M.D., M.P.H., is program director for the Women's Reproductive Health Research Program at the University of Washington in Seattle, Washington. She is a clinician at Harborview

Medical Center and University of Washington Medical Center. Dr. Reed is also an affiliate investigator at the Center for Health Studies and Fred Hutchinson Cancer Research Center, and an associate professor of obstetrics and gynecology, and an adjunct professor in epidemiology at the University of Washington School of Medicine. Dr. Reed's areas of clinical and research interest are gynecologic issues for women with genetic diseases, cross-cultural medicine, and management of menopause.

Dr. Reed received her master's degree (M.S.) in human genetics from Sarah Lawrence College in Bronxville, New York, her medical degree (M.D.) from Stanford University Medical Center in Stanford, California, and her Master of Public Health (M.P.H.) degree from the University of Washington School of Public Health. Dr. Reed is a licensed genetic counselor and board-certified in obstetrics and gynecology.

Jerry Richard Shields, M.D., is an ophthalmologist in private practice in Tacoma, Washington. He sees general ophthalmology patients and performs laser correction and cataract surgery. Dr. Shields is board-certified in ophthalmology and VISIX-certified.

Dr. Shields received his bachelor of science (B.S.) degree in biology *cum laude* from Wake Forest University in Winston-Salem, North Carolina, and his medical degree (M.D.) from the Medical College of Georgia in Augusta, Georgia. He completed his internship in internal medicine and his residency in ophthalmology at the University of Washington in Seattle, Washington.

Christina M. Surawicz, M.D., is gastroenterology section chief of at Harborview Medical Center in Seattle, Washington. She is also professor of medicine and assistant dean for faculty development at the University of Washington School of Medicine in Seattle. Dr. Surawicz is widely published in peer-reviewed journals and has authored, edited, and contributed to dozens of books.

Dr. Surawicz received her undergraduate degree, a bachelor of arts (B.A.) in biology, from Barnard College in New York City and her medical degrees (M.D.), awarded with honors, from the University of Kentucky College of Medicine in Lexington, Kentucky. She completed her medical internship, medical residency, and gastroenterology fellowship at the University of Washington in Seattle. Dr. Surawicz is board-certified in internal medicine and gastroenterology.

Denise L. Wych, R.N. C.M., is a cardiac nurse case manager at Palmetto Health-Richland Heart Hospital in Columbia, South Carolina, where she integrates clinical and medical appropriateness criteria in discharge planning and resource utilization within the framework of an interdisciplinary health-care team. She has worked in medical-surgical, intensive care unit, newborn, school nursing, and home health.

Ms. Wych received her diploma in nursing from Providence School of Nursing in Sandusky, Ohio. She served 10 years as an officer in the US Navy Nurse Corps, during which she was twice awarded the Navy Achievement Medal.

CUMULATIVE INDEX TO VOLUMES 1–4

Volume numbers appear in **bold** followed by a colon and the relevant volume page reference. Pages in **bold** indicate major treatment of a topic. Pages with a *t* indicate tables.